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THE PLACE OF IODINE IN THE TREATMENT OF GOITER*

BY HOWARD M. CLUTE, M.D.,† AND LEWIS S. PILCHER II, M.D.†

WITH the advent of the use of Lugol's solution for the preparation of patients with exophthalmic goiter for operation, and with the development of goiter prophylaxis by the use of iodine, there was a natural tendency to give iodine to any patient with a thyroid enlargement, with the hope that iodine would act upon it in a favorable manner. With increasing experience in the management of thyroid disease it became apparent that iodine was not a "cure-all" for every type of goiter. A number of reports have called attention to the fact that there are definite and distinct limitations in the use of iodine in thyroid diseases. We have previously reported the great benefits which consistently follow the proper administration of iodine in selected cases of thyroid disease and the futility of its administration in other types of goiter[1, 2]. In spite of the reported experiences of many authors, we have observed in recent years that iodine is still given indiscriminately to any type of goiter; and that there is apparently no diminution in the frequency with which this practice is followed in all types of goiter.

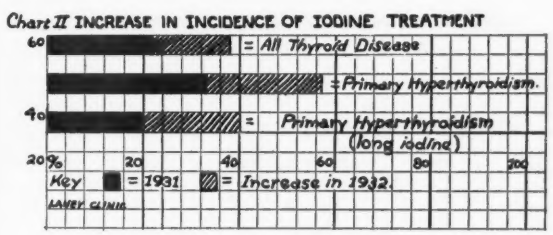
In order to ascertain how frequently iodine is given, we reviewed all the patients admitted to the Clinic in the month of January, 1931, who had or were suspected of having any type of thyroid disease, and we compared this group with the patients who entered the Clinic during the month of January, 1932. In January, 1931, one hundred and sixty-three patients were admitted to the Clinic for suspected thyroid disease, and one hundred and twenty-one of this number were found to be suffering from some form of goiter. In January, 1932, one hundred and fifty-two cases were admitted to the Clinic with suspected thyroid disease and ninety-five of these patients were found to have some type of goiter. (Table I.) In January, 1931, twenty-two per cent of the goiter cases had been treated with iodine before entrance and in January, 1932, thirty-eight per cent of the patients had received preliminary iodine treatment. (Chart II.) In the two hundred and sixteen cases of goiter seen in these two months, thirty per cent had been treated with iodine before entrance to the Clinic.

Not only is iodine being widely given in the treatment of thyroid disease, but also it is not carefully selected with a view to the type of patient who presumably will be benefited by iodine. It is our observation that any patient who has any type of thyroid disease, real or only suspected, stands a strong probability of receiving a "course" of iodine treatment before being referred for surgery. As would be expected, those patients who have true hyperthyroidism are more frequently given iodine. Thus, in these two representative months that we have chosen, forty-five per cent of all the patients with exophthalmic goiter had taken iodine before admission. Sixty-two per cent of the patients with adenomatous goiter and secondary hyperthyroidism had taken iodine. Nineteen per cent of the non-toxic single and multiple adenomatous goiters had been given iodine and twenty-five

TABLE I

CASES OF SUSPECTED THYROID DISEASE ADMITTED TO THE LAHEY CLINIC IN JANUARY, 1931, AND JANUARY, 1932

	January 1931	January 1932
Suspected Thyroid Disease	163	152
Real Thyroid Disease	121	95
No Thyroid Disease	42	57
Toxic Thyroid Disease	47	43
Primary Hyperthyroidism	30	38
Secondary Hyperthyroidism	8	5
Recurrent Hyperthyroidism	9	0
Non-Toxic Thyroid Disease	74	52
Colloid Goitre	8	5
Adenomatous Goitre	29	24
Discrete Adenoma	33	21
Carcinoma	1	1
Thyroiditis	3	1

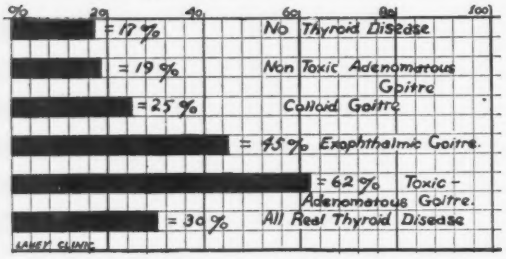


*From the Surgical Department of the Lahey Clinic, Boston, Mass.

†Clute—Surgeon, Lahey Clinic. Pilcher—Fellow in Surgery, Lahey Clinic. For records and addresses of authors see "This Week's Issue," page 162.

per cent of the colloid goiters had received it. Most interesting in this group is the large number of patients totalling nearly one-third of all admissions for suspected thyroid disease, who were found to be suffering from no disease of the thyroid gland. Seventeen per cent of this group, however, had been treated with iodine before coming for examination. (Chart I.)

Chart I INCIDENCE IODINE TREATMENT IN REAL AND SUSPECTED THYROID DISEASE



In January, 1931, one patient with cancer of the thyroid gland was seen and one patient with cancer was also seen in January, 1932. It so happens that each of these patients with malignancy had been given a "course" of treatment with iodine; one eight months and the other two years before entrance. It is apparent from these figures taken from the admissions in two widely separated months that the frequency with which preliminary iodine medication is given to real or suspected thyroid patients is not decreasing and for this reason it would seem desirable to review briefly the benefits which we may hope to derive from iodine therapy in thyroid disease and to point out the dangers which are latent in ill chosen iodine administration.

Iodine is of generally recognized value in preventing the development of endemic goiter. For the prophylaxis of endemic goiter only minute quantities are necessary, since one need only supply the small amount of iodine which the individual normally acquires from the drinking water and from the food in non-goitrous areas of the country. In a goiter belt in which the iodine content of the food and water is abnormally low, adequate prophylaxis of thyroid enlargements may be obtained by the administration to children coming to adolescence of a minute quantity of iodine once each week. We have used a chocolate-coated tablet containing one-sixth of a grain of iodine. These are sold in boxes of fifty for a very moderate price and in that way a year's medication at a dose of one chocolate-coated tablet per week is supplied. The administration of these minute quantities of iodine to children, particularly female children, growing to adolescence in goiter areas should be started a year or more before the time that their menstruation is anticipated and then maintained for a year or more after the menstrual function is well established.

Mothers known to have endemic goiters may well be given small doses of iodine in this same way, during the course of any pregnancy. This will not only prevent the mother's goiter from enlarging during her pregnancy but will also prevent the occurrence of thyroid enlargements in the baby.

The second place in which we must consider the use of iodine in goiter is in those individuals in whom goiter, of whatever kind it may be, is already apparent. In adolescent girls who have already developed small colloid goiters it is our practice to give this same prophylactic dose of iodine for a year or two with the hope that this will prevent further hypertrophy and colloid storage in the already enlarged thyroid gland. It is difficult, if not impossible, to prove that the administration of such small doses of iodine does prevent further growth of the thyroid. It is certain that in some cases the thyroid continues to grow in spite of it, but it appears equally certain that in many other cases further enlargement of the thyroid is checked. Since the administration of this small amount of iodine does no harm in the presence of early colloid goiter we favor its administration in these patients.

Iodine is of great value in the preparation of patients with hyperthyroidism for the surgical removal of the thyroid gland. This is well known since Dr. H. S. Plummer introduced the use of Lugol's solution in exophthalmic goiter in 1923[3], and the striking changes which occur in the severely toxic, exophthalmic goiter patient, after the administration of large doses of Lugol's solution for a week or ten days is well recognized. In this capacity of preparing patients with hyperthyroidism for operation, Lugol's solution has been of inestimable value. Before the use of Lugol's solution in this Clinic, sixty-two per cent of our toxic patients were done in multiple stage operations; now only twenty-two per cent of our patients require more than one operation for their thyroidectomy. Patients who formerly developed the crises of exophthalmic goiter with diarrhea, vomiting, extreme activation, fever, delirium, coma and death are now in most instances controlled by the administration of Lugol's solution and other supportive measures. Lugol's solution has proved of great value in the management of certain rare patients who, following thyroidectomy for exophthalmic goiter, have mild residual toxic symptoms. However, it must be stated that its administration postoperatively does not prevent recurrence of hyperthyroidism in certain cases.

Lugol's solution reduces the metabolism, controls the activation, slows the pulse rate, and generally improves patients with toxic adenomatous goiters. It is our experience that Lugol's solution is beneficial in temporarily improving the hyperthyroidism of adenomatous goiter just

as it is in exophthalmic goiter. We believe all toxic patients should be prepared for operation by the administration of Lugol's solution and have no hesitation in giving it in hyperthyroidism regardless of the type of goiter that is present.

The last place in which iodine is useful in the management of thyroid disease, and this occurs but very rarely even in those clinics which see large numbers of patients with hyperthyroidism, is in the diagnosis of certain border-line cases. It is well recognized that patients with neurocirculatory asthenia present a clinical picture not unlike patients with mild hyperthyroidism. To differentiate these two conditions is sometimes difficult. In true hyperthyroidism iodine lowers the basal metabolism, slows the pulse rate, diminishes the tremor and activation, increases the sense of well-being and permits a gain in weight. In neurocirculatory asthenia none of these effects are seen after using iodine. A marked improvement following the use of Lugol's solution marks the patient out at once, therefore, as, in all probability, suffering from hyperthyroidism and not from neurasthenia. It must be again emphasized, however, that these border-line cases requiring the use of Lugol's solution for their diagnosis are extremely rare.

After a considerable experience in the treatment of patients with thyroid disease, we have concluded that only two general indications are present in this disease for the administration of iodine; first, as a means of prophylaxis against the development of endemic goiter and secondly, in the management of hyperthyroidism preparatory to operation.

What harm may come from the administration of iodine to other types of goiter and for other purposes than those which we have enumerated above? There has, in the past, been much discussion in the literature concerning the production of hyperthyroidism by the administration of iodine to non-toxic adenomatous goiters. This question of the production of hyperthyroidism by giving iodine to a patient with simple colloid goiter or to a patient with a discrete or multiple adenomatous goiter is most difficult to settle. In repeated discussions on this point in the Clinic it is the consensus that we have yet to see a patient in whom we felt that there was any direct or adequate proof that hyperthyroidism had developed as a result of iodine administration. It is interesting to note that in the toxic adenomatous goiters seen in the two months which we have studied for this report, hyperthyroidism had clearly been present in every case but one before iodine administration was undertaken. Furthermore, it is to be noted even in this small group of patients that though iodine had been given very consistently in nineteen per cent of the non-toxic patients no toxicity was observed. From the point of view then of the possibility of producing hyperthyroidism we have no fear in administering iodine to non-toxic goiter patients.

The administration of a drug, however, should not be undertaken unless one has some definite objective in mind. Our experience is that iodine administration in non-toxic goiters will occasionally reduce the size of the goiter to a slight degree. This reduction in size, however, is not permanent in spite of the continued administration of the iodine. Furthermore, in certain nodular goiters, which are well recognized as premalignant lesions in a definite percentage of cases, the time spent in the administration of iodine, which it is well known cannot reduce the size of the goiter appreciably, may well be ill-advised in view of the possibility that malignancy may be present. The chance of early operation so necessary for the eradication of malignancy is lost while iodine is administered. This occurred in both of the cancer cases present in this group of thyroid patients so that one patient delayed two years and the other eight months, the surgical removal of malignant tumors. If it is recognized that iodine will not make an adenoma of the thyroid disappear then it is unfair to the patient to spend time with this type of treatment.

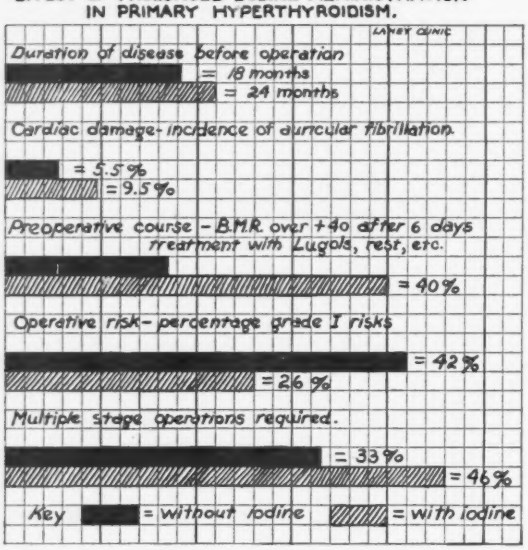
It must be strongly emphasized that iodine does not cure hyperthyroidism. The studies of Neisser, Loewy and Zondek, Thompson, Marine and others[4, 5, 6, 7], as well as our own experience[1] show that iodine continued weeks, months, and years, does not cure hyperthyroidism. In the group of patients whom we are considering there were several who had taken iodine for over a year before admission, and some for as long as three to five years, without curing their hyperthyroidism. In the past we have seen numerous patients who have taken iodine for many years without controlling their thyroid intoxication.

We have repeatedly demonstrated by carefully controlled studies of the metabolisms and by mortality statistics that surgery is a safe, quick, and sure method for the cure of hyperthyroidism[2]. The longer the hyperthyroidism persists, whether it be partially controlled by iodine or not, the more serious the disease and the more dangerous the surgery. We are completely satisfied that it is wrong to give patients with hyperthyroidism, whether it be due to exophthalmic goiter or to adenomatous goiter, iodine for long periods of time before insisting upon the surgical treatment.

In the ninety patients with hyperthyroidism seen in the two months which we are considering, iodine was known to have been given for more than a month in at least one-third of all the exophthalmic goiter cases and in one-half of all the toxic adenomatous goiters. Examination of the records of these patients shows that they

were sicker than the average, that they were poorer operative risks, and that they more frequently required multiple stage operations for their cure. (Chart III.) Thus, in these exophthalmic goiter patients the disease had been present for an average of two years in those patients who had a long iodine administration before entrance—six months longer than the average duration of the disease in those patients who had received no iodine. Auricular fibrillation was taken as definite evidence of cardiac damage and was present in nine per cent of the patients with long iodine administration while it was present in only six per cent of those who had not received iodine. Patients who had not received iodine before admission were considered excellent operative risks in forty-two per cent of the cases, but only twenty-six per cent of those who had received long iodine were considered good operative risks. Patients who had been given iodine before admission reacted poorly to preoperative treatment with iodine, rest, and sedation. In forty per cent of these patients the basal metabolic rate could not be brought below plus forty, while in patients who had received no iodine previously the basal metabolic rate was brought below plus forty in all but seventeen per cent of the cases. The only mortality that occurred in the two months under consideration occurred in a woman who had taken large amounts of iodine for over six months before entrance, who was in a serious crisis and who died of the toxemia of exophthalmic goiter without operation. She had passed through the initial stage of improvement which came following the first administration of iodine, at which time operation could have been undertaken with relative safety, and had gone into a crisis from which recovery was impossible.

Chart III
EFFECT OF PROLONGED IODINE ADMINISTRATION IN PRIMARY HYPERTHYROIDISM.


LAHEY CLINIC
Duration of disease before operation
= 18 months
= 24 months
Cardiac damage- incidence of auricular fibrillation
= 5.5%
= 9.5%
Preoperative course - B.M.R. over +40 after 6 days treatment with Lugols, rest, etc.
= 40%
Operative risk - percentage grade I risks
= 42%
= 26%
Multiple stage operations required.
= 33%
= 46%
Key = without iodine = with iodine

We are convinced that the long-continued administration of iodine in hyperthyroidism increases the risk of surgery as it prolongs the duration of the hyperthyroidism. It decreases the operability of the individual so that a subtotal thyroidectomy in one stage is less frequently advisable. It increases the chance of fatality from hyperthyroidism itself and it gives inevitably a longer period of total disability from the disease.

Conclusion: Iodine in small doses is of the greatest importance in the prevention of endemic goiter in adolescent children living in goiter belts. Iodine is of the greatest value in the preparation of patients with hyperthyroidism whether it be primary or secondary for the surgical removal of the thyroid gland. Iodine may do considerable harm in misleading the patient and postponing, in certain cases, the necessary surgical measures in potentially malignant non-toxic goiters. The administration of iodine for long periods of time in hyperthyroidism does great harm in increasing the risk of surgery, the number of operations necessary for the relief of the patient, and in the prolongation of the patient's disability.

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THE PHASES OF FOREIGN PROTEIN SENSITIZATION IN HUMAN BEINGS*

BY T. DUCKETT JONES, M.D.,† AND JOHN R. MOTE, A.B.†

NUMEROUS workers have attempted to use the skin reaction in determining the etiological agent in various diseases. The work of Birkhaug[1] (1927) was the first to call attention to the high percentage of positive skin reactions to streptococcal products in rheumatic fever. Since then Kaiser[2], Swift et al[3], Irvine-Jones[4], Coburn[5], Derick and Fulton[6], and Keefer et al[7] have done further work on this approach to the rheumatic problem. In these reports, in spite of the variety of materials used, as well

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as their widely differing concentrations, there is a consistently higher percentage of positive skin reactions in rheumatic fever subjects than in the case of normal individuals. In view of these findings, as well as the close clinical relationship between acute upper respiratory infections and rheumatic recurrences, a more detailed analysis of this streptococcus sensitivity was considered worth while. A better knowledge of this reactivity may be important in determining if an allergic mechanism is responsible, or whether the sensitivity is a concurrent and incidental phenomenon really unrelated to the disease process itself.

It seemed desirable in obtaining a skin testing substance to have the bacteria broken down in a physiological manner similar to that which might be expected to occur in the body normally. Under such conditions it is possible that the organisms are lysed with the protein and protein-carbohydrate chemical and special arrangements relatively unaltered, thereby giving bacterial products of perhaps more specific nature than can be obtained by severe chemical or physical treatment. To do this, experiments similar to those of McJunkin[8], and of Duval and Hibbard[9] were undertaken. An immunized rabbit was injected intraperitoneally with a large dose of living homologous hemolytic streptococci. Three hours later the peritoneal fluid was removed and a sterile Berkfeld N filtrate prepared. The skin test (intracutaneous) dose used was 0.1 cc. of 1:1000 dilution (0.0001 cc.) of this peritoneal filtrate. As a control material a similar filtrate was prepared following the intraperitoneal injection of a comparable amount of physiological saline in normal rabbits. It was thought that in the dilution used there was probably no danger of encountering foreign protein sensitization.

The streptococcal products thus obtained gave a high percentage of positive skin reactions when injected intracutaneously in rheumatic fever subjects. Although the percentage of positive reactions to the products of different strains of streptococci were consistently high, the same individuals were not sensitive to all strains. These results seemed to justify more extensive study of the skin sensitivity in rheumatic fever.

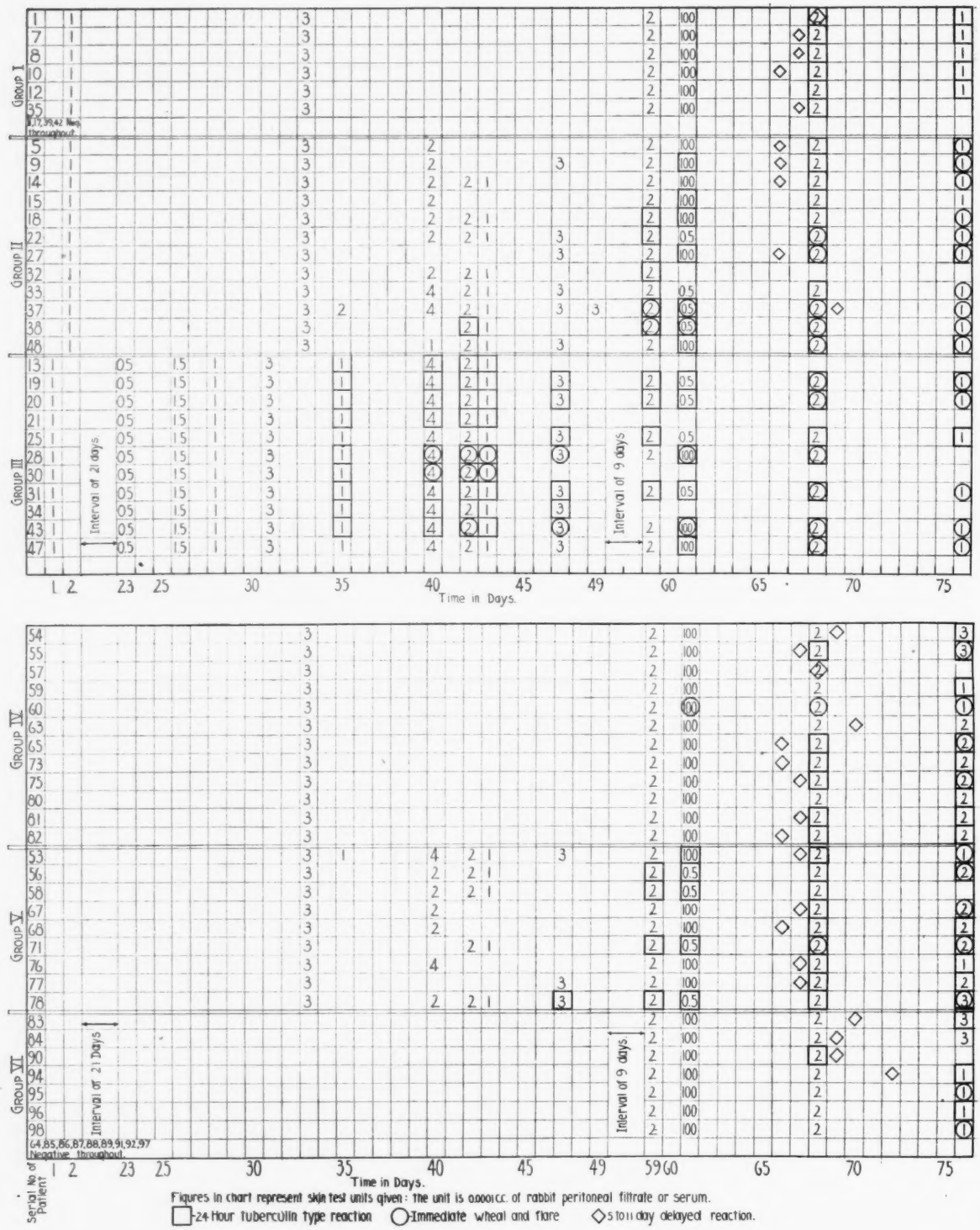
In a small series of tests it soon became obvious, from the type of reaction, that we were dealing with another factor in addition to the streptococcus reaction. When first tested none of the subjects in the experiment gave any skin reaction whatever to the normal rabbit protein in the dilution used. By controlling the test material with the peritoneal fluid and serum of normal rabbits in the same dilution, it was found that the group (see group III, chart) who had had repeated skin tests all reacted with typical 24 nour tuberculin type reactions to these normal rabbit proteins. After the 24 hour type sensitivity to the protein had developed, a few additional injections of rabbit proteins resulted in the development of an immediate wheal with a residual 24 hour reaction. Finally, as the individual became more sensitive from continued tests there was only a large immediate wheal and flare reaction with little or no trace of the injection area after 24 hours. The 24 hour type sensitivity was not transferable by the Prausnitz-Kustner technic, whereas the immediate wheal sensitivity was transferable.

These observations indicate that the first evidence of foreign protein sensitization as detected in the skin is a 24 hour tuberculin type reaction. As the hypersensitivity increases the typical immediate wheal of foreign protein sensitivity appears.

Furthermore, at the site of injection of 0.01 cc. of rabbit serum there was observed a much delayed reaction (between the fifth and eleventh day). In some cases there arose a large urticarial wheal which appeared quickly and was present at most for only several hours. In the majority of instances there developed a diffuse, red, well circumscribed, edematous reaction which faded more gradually (24 to 48 hours). These reactions are considered to be essentially local serum disease.

From an analysis of the accompanying chart certain facts are apparent:

1. The 24 hour tuberculin type reaction is the first to be elicited in nearly every case where repeated small doses were used (see groups II, III and V).
2. There is a tendency for a progression in the same individual from the 24 hour type reaction to an immediate wheal plus a residual 24 hour reaction. Later, in the more highly sensitive subjects only an immediate wheal and flare with little or no residuum results.
3. In only three (3) instances was the immediate wheal the first reaction to develop.
4. Sensitization with small amounts of protein would seem to depend more on the interval between tests than on the actual amount of material injected (compare Groups I, II, and III, and Groups IV and V in Chart).
5. When fifty-three (53) individuals were injected with 0.01 cc. of rabbit serum intracutaneously twenty-eight (28) (52.8%) developed, at the site of injection, the greatly delayed (5 to 11 days) type of reaction described above. Of these twenty-eight (28) subjects, the first evidence of sensitivity in twenty-two (22) instances was this reaction (see Groups I, IV and VI).
6. The groups were formed on the basis of the number of tests given. The similarity of reactions of the members of the same group is striking.
7. Of seventy (70) subjects in the experiment, fifty-seven (57) (or 81.4%) became hypersensitive to rabbit proteins during the period of observation.


Group I
Group II
Group III
Group IV
Group V
Group VI
Interval of 21 days
Interval of 9 days
Time in Days.
Serial No. of Patient
Figures in chart represent skin test units given: the unit is 0.0001 cc. of rabbit peritoneal filtrate or serum.
24-Hour tuberculin type reaction
Immediate wheal and flare
5 to 11 day delayed reaction.

Results of intracutaneous injection of rabbit proteins in 70 patients. No tests were given during the longer intervals noted on the chart. Where no further tests are represented the patient was discharged from the hospital during the course of the experiment.

DISCUSSION

Since this is a preliminary report a full discussion will not be attempted. At the present time the relation of precipitins and passive transfer to the above phenomena are being studied. In addition, after an interval of eight months these patients are being retested. These results will be reported in a more complete paper in the near future.

In this series of individuals, the demonstra-

tion of development of sensitivity with such minute amounts of protein used as sensitizing doses, has been striking and at direct variance to the impression that human beings are rather refractile to foreign protein sensitization. It may be that the intradermal mode of administration as well as the small doses used, are in part responsible for the results observed. It is true that different proteins vary greatly in their antigenic properties and that many of them are very weak antigens (particularly denaturized proteins). Since human beings are so easily sensitized to foreign protein, the casual relationship between the skin reactions and a disease condition may be impossible to establish.

From the observed events that have taken place in this experiment, there is evidence substantiating the theory that all of the allergic phenomena have a very similar if not identical basic mechanism. Furthermore, the progression of events as seen in the Chart seems to indicate that the difference between tuberculin type of allergy and the hypersensitiveness to foreign protein is a quantitative and not a qualitative one.

From consideration of groups II, III, and V (individuals who had numerous skin tests), it would seem that the sensitizing process is a natural one once the protein is introduced into intimate contact with tissues.

The greatly delayed type of reaction which developed after the intracutaneous injection of 0.01 cc. of rabbit serum may be considered as a local serum disease since it is similar in type as well as in time interval to the skin manifestations of serum disease.

CONCLUSIONS

1. The quantitative relationship between tuberculin type of hypersensitiveness to foreign protein and typical foreign protein sensitization as observed in the skin has been experimentally studied in human beings.
2. Human beings have been inadvertently sensitized with very small amounts of rabbit protein. Only 0.0003 cc. was necessary in one case, and in nine (9) instances as little as 0.0007 cc. of rabbit peritoneal fluid or serum were effective as sensitizing doses.
3. The earliest indication of foreign protein sensitivity in the skin when small sensitizing doses are used is a 24 hour tuberculin type reaction.
4. Where the cause of a disease process is not already established it may be impossible to evaluate the etiological significance of skin sensitivity to proteins.

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GASTRO-INTESTINAL ALLERGY ASSOCIATED WITH TRANSIENT INTRAVENTRICULAR BLOCK

BY JAMES C. HEALY, M.D.,* DAVIS T. GALLISON, M.D.,* AND JAMES BRUDNO, M.D.*

THE authors desire to present this case because of the unusual etiological association of high-grade eosinophilia, gastro-intestinal allergy, and intraventricular block, together with rapid clinical improvement under a new form of therapy.

Z. B., a 46 year old male pastry-cook, unemployed for several months, was admitted to the Third Medical Service of the Boston City Hospital on January 21, 1933. His complaints at entrance were colicky abdominal pain, diarrhea, and tenesmus. The past history was negative, except for an attack of acute rheumatic fever at the age of 13. Since then he had had transient joint pains but had no symptoms referable to the cardiovascular or gastro-intestinal systems. In fact the patient disposed of the questioning about his previous illnesses and regional history by insisting with emphasis that his health always had been perfect.

Family and marital history revealed no pertinent information. Blood examination of one child, who arrived at the hospital to visit his father, showed a ten per cent eosinophilia. Although there was no history of allergic phenomena, skin tests were done, and a one plus positive reaction to three food-proteins resulted.

The present illness began three weeks ago. At that time he had severe upper abdominal pain, nausea, vomiting, and constipation. These lasted two days. The pain then became localized in the periumbilical and lower abdominal regions and was accompanied by diarrhea and tenesmus. The stools were light in color, foul, painful, and numbered eight to twelve a day. He noticed no blood, pus or mucous shreds and could recall no association be-

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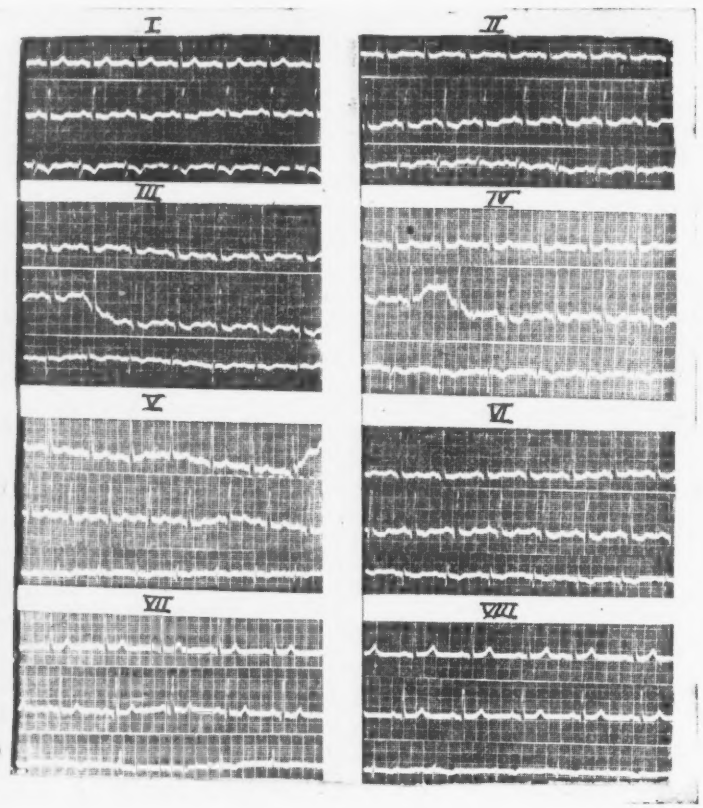
tween abdominal pain, defecation, and ingestion of food. Appetite was greatly impaired, and for two weeks the diet had consisted only of small amounts of liquid.

Physical examination at time of admission revealed a fairly well-developed and nourished white Italian not acutely ill. The skin was dry, and the mucous membranes were parched but of good color. Head and scalp were normal. The pupils were small, equal, and reacted well to distance but poorly to light. The sclerae were normal. There was moderate pyorrhea; the teeth were in poor condition and the tongue was coated. The pharynx, nasopharynx, and larynx revealed no abnormalities. There were no visible pulsations or adenopathies of the neck.

By percussion, the heart was found to be questionably enlarged to the left. The sounds were regular and of good quality. The rate was ninety per minute. There was a soft systolic murmur at the mitral area, not transmitted. B. P. was 130/60. The lungs were normal.

The abdomen was moderately distended but not tender. The liver, spleen, and kidneys were not felt. There were no palpable inguinal glands. The reflexes and extremities were normal. The oral temperature was 99.8°F.

At the time of admission, the leucocyte count was 12,000 per cubic millimeter; the red corpuscle count was 6,000,000; the hemoglobin was 97 per cent by the Sahli method. The blood non-protein-nitrogen was 35 mgms. per 100 cc. The Kahn test was negative, and several urine examinations disclosed no abnormal findings. A urine concentration test was found to be within normal limits. Gastric analysis was negative, and a normal response to histamine was obtained. Three teleroentgenograms were taken, two of which demonstrated slight enlargement of the heart to the left; the third was normal. The lung fields were found to be clear on two fluoroscopic observations and films were consistently negative. Roentgenograms of the bones revealed no pathology, and a gastro-intestinal series was negative, although a barium enema disclosed increased haustral markings sufficient to warrant a diagnosis of spastic colitis.



All tracings—normal sinus rhythm.
Rate 63-85.
Slight left ventricular predominance in all except VII, in which the axis is normal.
PR interval varied from .16 to .20.
III, V, and VI show an intraventricular block.
Other abnormalities referred to in the text.

A sigmoidoscopic examination was undertaken, and redness of the anal lining and rectal mucosa noted. Smears from the mucous membrane were cultured, but no unusual organisms found.

A routine electrocardiogram (I in the reproduction) was taken on January 24, three days after admission. The significant abnormalities were slurring of $QRS^{1,2}$ notched QRS^{3}, diphasic T^{3}, and slight left axis deviation.

Shortly after the admission of the patient, the stools were found to contain occult blood, but this disappeared after a few days. Several cultures were made, but no unusual organisms were found. In repeated examinations neither parasites nor ova could be detected. There were, however, many eosinophilic leucocytes in several stools, which took not only the ordinary Wright's stain but also neutral red and Janus green by the supravital technique. With the latter dyes the eosinophiles were still motile in stools several hours old.

Blood serum agglutination tests for B. typhosus and paratyphosus A. and B. were repeatedly negative as were several blood cultures for the same organisms.

Provisional Diagnosis: Spastic Colitis.

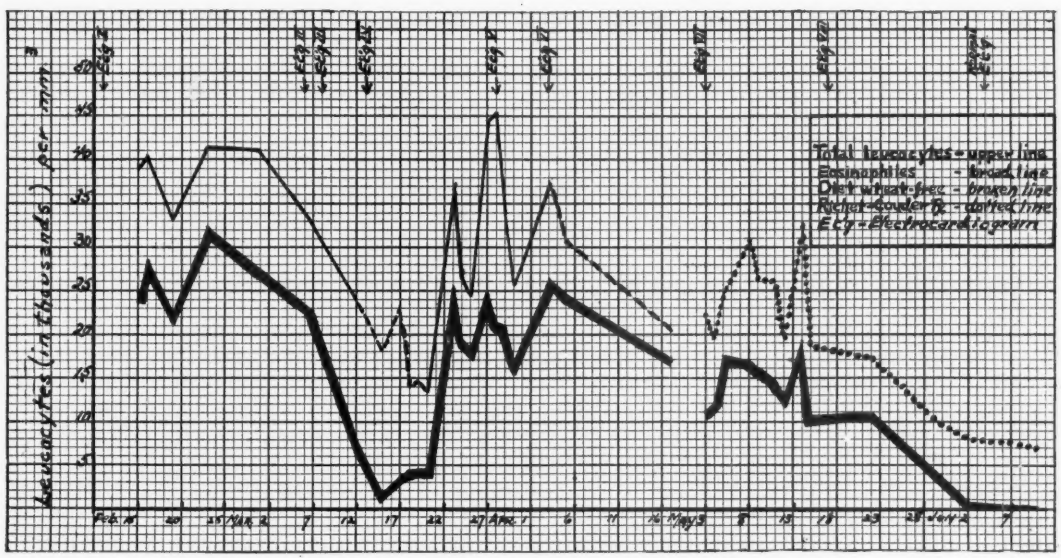
Treatment: The patient was given paregoric and bismuth subnitrate. Fluids were forced, and a soft solid diet prescribed.

Subsequent Course:

Shortly after admission of the patient the symptoms were relieved and the frequency of stools decreased. On the seventh day he was sigmoidoscoped. About this time the diarrhea and distress became less troublesome and the patient began to eat more. Three days later (February 1) he had thirteen stools in as many hours and complained of considerable abdominal colic. This persisted with varying intensity, and on the fifteenth of February it was found that his white count was 34,000, of which 70 per cent were eosinophiles. Precipitin cium was 9.5 mgms. per 100 cc. on March 7 but was found to be normal on March 19.

A diet excluding wheat was prescribed on March 7. During the next nine days the subjective symptoms of diarrhea and abdominal distress were markedly relieved. The total leucocyte count dropped, and the percentage of eosinophiles decreased to ten per cent. An electrocardiogram (III in the reproduction) taken on March 8, demonstrated an intraventricular block. The significant abnormalities in that tracing were diphasic $T^{1, 2}$ waves, inversion of T^3, slurring of $QRS^{2, 3}$ with a time interval of .12 second. Five days later after wheat had been eliminated from the diet and gastro-intestinal symptoms relieved another electrocardiogram (IV in the reproduction) showed no intraventricular block.

A week after the skin tests were done there was a typical attack of generalized urticaria with a sharp rise of the total white count and a slow rise of eosinophiles in the blood. The eruption lasted several days. Shortly after this the white count


Leucocytes (in thousands) per cmm.
Total leucocytes = upper line
Eosinophiles = broad line
Diet wheat-free = broken line
Richet-Couder Tx. = dotted line
Ecg = Electrocardiogram

Graph showing relation of total and eosinophilic leucocyte count to form of treatment and electrocardiographic records.

tests for trichiniasis were reported to be positive, but a biopsy examination of a bit of the deltoid muscle showed no evidence of infestation.

Because of the unexplained preponderance of eosinophilic leucocytes in the blood, the presence of the same cells with absence of all other blood elements in the stools[1], the normal temperature and the spastic colitis, tests for allergic disease were undertaken. By means of the dermal scratch and indentation techniques, it was discovered that the patient was hypersensitive to whole wheat, wheat gliadin, wheat leucosin, and wheat proteose. These conclusions were drawn after he had been tested with all the food proteins of his usual diet.

To rule out a possible eosinophilic type of leukemia, function tests of the hemopoietic system were done[2, 3]. Briefly, the results indicated that a response for eosinophiles, neutrophiles, and lymphocytes could be obtained by the specific stimulus for each.

Several blood non-protein nitrogen determinations were made, the results varying from 35 to 67 mgms. per 100 cc. The blood creatinin varied from 1.3 to 1.9 mgms., and the uric acid content 4.4 to 5.2 mgms. per 100 cc. The higher figures in the above findings were found to coincide with the peaks of eosinophilia as shown on the chart. The blood cal- and eosinophilia sharply rose and all symptoms recurred. After rigorous questioning the patient admitted his acceptance of toast from a sympathetic ward neighbor. An electrocardiogram taken at this time (V in the reproduction) showed a recurrence of the intraventricular block and diphasic $T^{1, 2}$ waves.

During the next two weeks the eosinophilia persisted, and the symptoms were more or less prominent. Despite attempts to supervise the diet, the patient had eaten a wheat cereal on several occasions. On April 15, when it was certain that he had not eaten any wheat for forty-eight hours, an electrocardiogram (VII in the reproduction) showed nothing but an inverted T^3.

Two days later the patient developed a strangulated inguinal hernia and was transferred to the Surgical Service for immediate operation. Convalescence after herniotomy was uneventful, and the patient was readmitted to the Medical Service on May 3.

Realizing the seeming impossibility of keeping the patient on an absolutely wheat-free diet, it was decided to attempt the form of treatment reported by Richet and Couder[4]. Before each meal the patient was given two teaspoonfuls of mineral oil and instructed to eat as little wheat as possible. Frequency of stools promptly decreased to one or two

a day; the abdominal cramps disappeared and he began to gain weight. The total white count and eosinophilia declined slowly, their course being graphically represented on the chart. A final electrocardiogram (VIII in the reproduction) showed only an inversion of T^3.

Two weeks after discharge the patient reported for a check-up. He was having one or two bowel movements a day and was entirely free of abdominal pain and discomfort. Since the institution of petrolatum therapy, he had regained twenty-nine of his thirty-one pound weight loss.

Diagnosis: Spastic Colitis
Gastro-intestinal Allergy
Intraventricular Block (allergic).

COMMENT

In making a diagnosis of allergic disturbance in this case, the authors found symptoms or signs which fulfilled Rackemann's[5] five essential requirements for such a diagnosis, namely, (1) a symptom which can be explained by smooth muscle spasm; (2) occurrence of other manifestations of allergy; (3) family history of allergy (presumptive in this case); (4) positive skin tests; (5) blood eosinophilia.

Contrary to the popular notion, alimentary reaction of the type reported in this case is most often due to food hypersensitivity[6, 7]. Colitis with spasticity of the colon and mucus in the stools has been reported to be of allergic origin in a large number of cases[8, 9, 10, 11, 12, 13, 14]. Gay[15] has reported that 21 of 32 cases of gastro-intestinal allergy showed by fluoroscopy a spastic colon and by proctoscopy a reddened anal canal and rectal mucosa. In these cases there were also positive skin tests to one or more of the protein extracts of wheat, eggs, beef, milk, corn, cocoa, rice, chicken, tomato, pepper, coffee, and vanilla. Furthermore, the presence of eosinophiles in the stools without other blood elements is evidence of gastro-intestinal allergy[1]. The high blood non-protein nitrogen and uric acid[16], low chloride and calcium content[17] have all been noted in experimental anaphylaxis and clinical allergy. In this case all these abnormalities disappeared with symptomatic relief.

In studying the heart changes in this case, as evidenced by the electrocardiograms, it is reasonable to explain the condition by evaluating the importance of the symptom of disease associated with it at the moment. Electrocardiograms I, II and III taken before the patient's wheat idiosyncrasy was discovered reveal definite conduction changes and evidence of coronary disease. Tracing IV (taken after wheat had been eliminated from the diet) reveals no block, but the diphasic $T^{1, 2}$ and left axis deviation are still present. Numbers V and VI (taken after the patient had broken his diet) are similar to those obtained before dietary restrictions were imposed. Tracing VII (recorded after his food had been free of wheat for several days) reveals a distinct improvement, while number VIII (taken shortly before discharge) shows only a slight left axis deviation. Another electrocardiogram not reproduced (taken a month after discharge) was normal.

Osler[18] in the Lumleian Lecture mentioned the possible allergic nature of angina pectoris with its spasm of the coronary arteries and ischemia of the myocardium. He also drew attention to the high incidence of this malady among the well-fed and particularly stressed its familial tendency. Certainly, no disease or condition has a greater familial incidence than allergy in some one of its manifestations. Dumas[19] drew attention to those cases of angina which are unexplained by the lack of organic changes in the vessel wall. These he considers to be of allergic origin in which the smooth muscle of the coronary artery becomes spastic just as the bronchiolar muscle would in asthma. Furthermore, he believes that frequent attacks or chronic spasm of this kind play an important rôle in the evolution of coronary disease. Werley[20] reported sixty-two cases of angina pectoris and coronary disease, all but 3.2 per cent occurring in allergic individuals. One case related by him concerns a patient who suffered anginal attacks during a siege of migraine and angioneurotic edema. He had had periodic attacks of colitis for several years. Electrocardiograms taken during the attack revealed an inversion of the T waves, and these returned to normal with relief of the allergic condition. As has been pointed out, the mechanism of these attacks is vessel spasm, and the probable site is the coronary arteriole. In those cases where there is coronary thrombosis, an allergic phenomenon cannot be excluded as an etiological factor. In addition to spasm of the vessel with narrowing of its lumen, there is a predisposition to intravascular thrombus formation because of the increased viscosity of blood. The latter has been observed in anaphylactic states[21].

Going a step further Duke[22] reported his observations on cardiovascular changes in hypersensitivity, particularly those resulting from physical allergy. He has shown that it is easy (in sensitive persons) to induce angina pectoris, tachycardia, and ventricular extrasystoles by the application of heat or cold to the precordium. Adrenalin rapidly caused relief of anginal symptoms and the disappearance of rate and rhythm changes.

Evidences of allergy resulting from the ingestion of wheat occurring for the first time so late in life seemed to be improbable at first glance. Several factors should be considered, however: first, the amount of wheat ingested; secondly, the form ingested; thirdly, the degree of hypersensitivity; and finally, the accuracy of the patient's history as to previous health and onset of present illness. Smul[23] has recorded the fluctuations of hypersensitivity to any protein. A patient may have mild abdominal symptoms and call it "indigestion", the symptoms being more or less fleeting. He has observed that such a patient may eat the allergic foods during

a period of latent sensitization without any reaction. Then when he becomes sufficiently sensitive he will have an attack of distress after eating the offending protein. Furthermore, the degree of sensitivity appears to affect quantitatively and qualitatively the resulting allergic phenomena.

In regard to the chemical nature of the allergen ingested, physical agents such as heat in one form or another can change a protein and make it more or less easily absorbable in a form calculated to produce a reaction. For instance, a protein subjected to dry heat will still have an allergic effect when administered to a sensitive individual[24]. This patient, Z. B., had been accustomed to eat a form of bread which (in the process of cooking) was treated with superheated steam. Shortly before the onset of his illness, he was put on the welfare list of the city. Consequently, the character of his diet was radically changed. The bread obtained under these circumstances and in the hospital ward was not made in the manner to which he had been accustomed.

Originally, the treatment of this case was the complete exclusion of wheat in all forms from the diet. Because of the patient's desire for wheat, because of the sympathetic ward neighbors who gave it to him, and because of the economic problem to be solved after his discharge, the treatment described by Richet and Couder was started. This consists of the use of mineral oil taken by mouth before meals, the theory being that the oil decreases or prevents the absorption of the products of incomplete protein digestion. These latter fractions are said to be the allergens which cause the manifestations of hypersensitivity. Actually, the patient failed to show much improvement until this oil therapy was begun. Thereafter, he gained weight rapidly and was able to eat foods containing wheat flour.

SUMMARY AND CONCLUSIONS

A case of allergic colitis with intraventricular block is presented. Wheat was found to be the offending allergen, and with its elimination from the diet the patient improved temporarily. As complete adherence to the diet was impossible, the condition recurred. Mineral oil given before meals proved to be the effective remedy in checking the allergic phenomena and resulted in a cure of the patient's gastro-intestinal and cardiac disturbances.

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THE ASSOCIATION OF DIABETES AND TUBERCULOSIS*

III. Clinical Features

BY HOWARD F. ROOT, M.D.†

1) Selection of Cases.
2) Clinical Course of the Diabetes, age at onset, changes in weight and acidosis.
   a) Glycosuria and Tolerance.
   b) Blood sugar.
   c) Cholesterol.
   d) Severity.
   e) Diabetic metabolism before the development of tuberculosis.
3) Clinical Course of Tuberculosis in Diabetics, onset, physical signs, and symptoms.
   a) X-ray examinations.
   b) Interpretation of roentgenograms in 89 cases.
4) Diagnosis.
   a) Intracutaneous tuberculin tests.
   b) Physical signs.

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5) Clinical forms.
6) Childhood and adolescence.
7) Old age and tuberculosis long latent.
8) Rate of progression.
9) Complications.

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1) Selection of Cases

THE 245 cases of this report were selected first as cases of true diabetes after the exclusion of all cases of renal glycosuria, transient and unclassified glycosuria.

For the diagnosis of true diabetes the following criteria have been the rule:

1. Glycosuria which varied in amount directly in proportion with alterations in the carbohydrate of the diet.

2. Hyperglycemia as indicated by a blood sugar in the fasting condition of 0.14 per cent or of 0.17 per cent or above with simultaneous glycosuria an hour after a full meal or following a glucose tolerance test. Failure of the blood sugar to return to a normal level two hours after a glucose tolerance test performed with 100 grams of glucose has been considered presumptive, but not definite proof of true diabetes.

3. The presence of characteristic symptoms has not been the rule; in fact, many patients with diabetes never have characteristic polyuria, polydipsia, and pruritus. Particularly in patients who already have some chronic emaciating disorder such as tuberculosis, the symptoms of mild diabetes may be insignificant and if small amounts of sugar in the urine are not thoroughly investigated the diagnosis of diabetes may often be missed. In one case of this series the patient was in an excellent tuberculosis sanitarium for nine months. The urine was tested once upon admission and showed 0.3 per cent sugar. She had had diabetes for at least three years, but the diagnosis of diabetes was never recognized during the nine months of her stay in the sanitarium. She began the use of insulin the next year and has continued it for 8 years.

Other factors make it easy for the presence of diabetes to be missed in the tuberculous patient especially in later years and after diabetes of some years' duration. The renal threshold may be elevated so that the urine may be sugar-free when the sugar of the blood is at a definitely diabetic level. With the development of arteriosclerotic nephritis the urine may become sugar-free. In cases of advancing tuberculosis and great emaciation, the urine may fail to show sugar.

Renal glycosuria is characterized by (a) constant glycosuria irrespective of diet, (b) absence of diabetic symptoms, and (c) a blood sugar which is invariably normal. Potential diabetics are those with glycosuria closely related to the diet, who become sugar-free easily, but whose blood sugar is below 0.14 per cent fasting and never exceeds 0.16 per cent after a meal.

For the diagnosis of pulmonary tuberculosis the following five points have been accepted:

1. Persistent medium or fine râles at either apex.

2. History of pleurisy with effusion. In but two cases was a diagnosis made on the basis of pleurisy with effusion alone, and in both subsequent examination and roentgenogram were positive.

3. Hemoptysis. In all cases positive roentgenograms were obtained.

4. X-ray evidence of mottling at the apex or beneath the clavicle.

5. Sputum containing tubercle bacilli.

In this series of 245 cases x-ray reports of tuberculosis are available in 153 cases. A number of the cases without x-ray films available for reexamination belong to the period preceding 1910. Most of the remainder were treated in tuberculosis sanitaria some years after they were examined for diabetes and I have not been able to secure x-ray data. In a few instances patients have come to the Deaconess Hospital from sanitaria for dietary adjustment only. I do not intend to convey the belief that all cases of pulmonary tuberculosis in the series of 10,000 diabetics have been discovered. Reasoning from the findings of 1659 consecutive chest films it seems clear that tuberculous infection has occurred in at least 70 per cent of diabetic patients. That many cases develop advanced processes in the lungs with little or no typical symptoms or physical signs has been amply demonstrated many times. How many more cases in this series died of pulmonary tuberculosis masked as pneumonia or influenza or who died of angina pectoris or gangrene during the course of pulmonary tuberculosis we have no means of knowing. Postmortem evidence is based on such a small series of hospital cases admitted for the most part because of acute or semi-acute surgical conditions that the autopsy statistics from the Deaconess Hospital and probably other general hospitals in the United States may be far too low.

Among the 245 cases are ten cases or 4.5 per cent which could be classified as having minimal lesions only, following the classification of the National Tuberculosis Association.

The Classification

Adopted by the American Sanatorium Association and the National Tuberculosis Association in May, 1930.

1. Minimal Lesion:
   a. Slight infiltration without demonstrable excavation.
   b. A small part of one or both lungs, and total volume of involvement, regardless of distribution, shall not exceed the equivalent of the volume of lung tissues which lies above the second chondrosternal junction and the spine of the fourth or body of the fifth thoracic vertebra on one side.

Symptoms.

A. Slight or none:
Slight or no constitutional symptoms, including particularly gastric or intestinal disturbance or rapid loss of weight; slight or no elevation of temperature or acceleration of pulse at any time during the 24 hours. Expectoration usually small in amount or absent. Tubercle bacilli may be present or absent.

B. Moderate:
No marked impairment of function, either local or constitutional.

C. Severe:
Marked impairment of function, local or constitutional.

Incipient pulmonary tuberculosis is rarely found in a diabetic. Tardy diagnosis is the outstanding feature of all diabetic tuberculosis and has probably colored many of the statements and opinions regarding the character of the process.

2) Clinical Course of the Diabetes.

Among the 245 cases of this series in 207 instances the onset of tuberculosis was subsequent to the onset of diabetes. In table 1 are shown

TABLE 1

245 Cases of Combined Tuberculosis and Diabetes

	0-4	5-9	10-19	20-29	30-39	40-49	50-59	60-69	70+
Ages at Onset of Tuberculosis		2	14	31	46	37	62	39	14
Ages at Onset of Diabetes	4	14	34	45	60	58	22	8	

the ages of onset for the two diseases in this series. In any discussion of the relative period of onset of the diabetes and tuberculosis, attention must first be called to the insidious type of onset of the two diseases. In older literature the words "acute diabetes" often appear and the impression is still current that the great majority of cases of diabetes have a rather sudden onset and that characteristic symptoms of diabetes are to be accepted as fixing the date of onset. On the contrary in the vast majority of cases of diabetes the onset is indefinite, gradual and the dates set for the onset of diabetes probably in most instances err on the side of being too late rather than too early. However, in the cases here reported painstaking efforts were made to ascertain with accuracy by questioning the family as well as the patient the date of the onset of such symptoms as polyuria, polydipsia, loss of weight and strength, and the first discovery of glycosuria. In only 58 cases were the symptoms of polyuria and polydipsia absent. In general, dates of onset of diabetes are more definitely established than the time of onset of tuberculosis.

Obesity in adults is the most frequent etiologic factor antedating the onset of diabetes. In this series of 245 cases similarly 80 per cent had been more than 5 per cent overweight before the onset of diabetes. The fact that they had been overweight prior to onset of diabetes suggests, but does not prove, that if pulmonary tuberculosis were present it was not active. In a few cases diabetes developed even though they were underweight. O'Donnell[2] studied cases of diabetes occurring in persons who had never been up to standard weight for age, height and sex. In this group tuberculosis as a cause of death was about three times as frequent as tuberculosis as a cause of death in Dr. Joslin's whole series, suggesting the presence of tuberculosis before the diabetes.

Great loss of weight was an outstanding feature in the majority of this series. The average loss of weight for 219 cases was 42 pounds. Loss of weight in excess of 75 pounds occurred in 19 cases and in five cases it varied from 100 to 125 pounds. The average loss of weight was 88 pounds in 9.5 years for 24 cases.

In 16 cases the loss began at or within one year of the onset of diabetes. In the other eight cases, the maximum weight was attained from two to 15 years prior to the onset of diabetes, but the greater part of the weight loss occurred after the onset of diabetes. In four of these eight, the patient could give no definite information as to whether any weight had been lost between the time maximum weight was attained, and the onset of diabetes. The long duration of gradual weight loss even before diabetes was clearly proved in four cases suggests the possibility that tuberculosis was already present even though no history of symptoms antedating the diabetes was obtained. In some instances a greatly restricted diet planned for the treatment of the diabetes was clearly responsible for part of the weight loss. For the majority active and uncontrolled diabetes clearly explained much of the weight loss. One cannot escape the conclusion that emaciation was a contributory factor in the development of active tuberculosis in many cases with an otherwise quiescent or arrested process.

Improvements in treatment have not only prolonged the life of the diabetic but enabled the diabetic child to grow to adult life and the diabetic adult to carry on community life in almost normal fashion. However, the diabetic is still a diabetic and periods of hyperglycemia and acidosis do occur. Fitz[3] quotes Wilder and Adams who stated that among the first thousand cases of diabetes treated at the Mayo Clinic after 1922, 29 entered with sufficient acidosis to produce a blood bicarbonate concentration of less than 25 volumes per cent. At the Deaconess Hospital from February 1, 1929 to September 1, 1931, 74 cases of coma with blood bicarbonate

concentration of 20 volumes per cent or below were admitted, or an average of 29 per year. The total diabetic admissions are about 1000 per year, and the incidence of coma in general diabetic admission was thus about three per cent

continued chronic infections not of tuberculous character, exemplified by Case No. 5608 who was in the Deaconess Hospital for three months with osteomyelitis of the hip. The following summary of her record in table 2 shows that

TABLE 2

IMPROVEMENT IN TOLERANCE DURING LONG-CONTINUED SEPSIS

Case Nos.	Age Yrs.	Duration of Diabetes Yrs.	Duration of Illness Days	Urine Sugar Per Cent	Blood Sugar Per Cent	Insulin Units	Result
5608	56	10	1	1.2	0.32	65	Osteomyelitis of hip
			6	0.5	0.28	35	
			31	tr.	0.11	25	
			32 to 73 inc.	0	0.15 to 0.20	0	Recovery
5317	62	0.3	1	4.5	0.39	65	Carbuncle
			12	tr.	0.24	30	
			18	tr.	0.20	15	
			31	0	0.18	0	
			32 to 71 inc.	0	0.17	0	Death from sepsis July 7, 1926
			86 to 126 inc.	0	0.16	8	

both at the Mayo Clinic and the Deaconess Hospital. Among the 245 tuberculous diabetics coma has occurred 37 times or five times as frequently as among the non-tuberculous diabetics.

a) Glycosuria and tolerance. The degree of glycosuria in the diabetic with pulmonary tuberculosis varies but little from that of the ordinary case. In these 245 cases the glycosuria varied from a trace to 11 per cent, the largest single group showing from three to four per cent. The old rule that when a diabetic patient is not doing well without any discoverable cause tuberculosis should be suspected, indicates that with advancing tuberculosis the effect upon the diabetes may be extremely unfavorable. The opposite effect has often been noted, that, as terminal stages of the tuberculosis are reached, the diabetes becomes very amenable to treatment and the glycosuria disappears. The sudden disappearance of glycosuria and development of hypoglycemia overnight with small doses of insulin occurred in Case No. 11471. During the next week, the urine was sugar-free and she was able to take 150 grams carbohydrate daily without insulin. A more gradual change is illustrated in the record of Case No. 344 reported by Joslin[4]. Umber[5] noted four such cases among 143 tuberculous diabetics. Peronne[6] and Schemensky[7] each noted a case with improvement in tolerance. Lundberg[8] based his belief that tuberculous tissue contained an insulin-like substance, para-insulin, upon improvements in tolerance which he observed in 14 cases of diabetic tuberculosis. Death from tuberculosis occurred in nine of his cases. His tables show very little increase in carbohydrate tolerance not accountable by increases in his insulin dosage. A similar effect is occasionally seen in long-

the urine became sugar-free for six weeks without insulin. Also Case No. 5317 with a carbuncle of the neck was able to give up insulin although metastatic infection of the knee-joint continued.

The carbohydrate tolerance is variable not only in different groups of patients but in the same patient. The estimated tolerance of 189 patients was obtained by subtracting from the total carbohydrate of the diet prescribed at the end of observation, the glucose in the urine for 24 hours and the glucose equivalent of the insulin dose on a basis of two grams glucose for each unit insulin. All estimations of tolerance are open to criticism. In this method no account is taken of the protein metabolism and of glucose derived from it. Similarly the possible glucose from fat either of the diet or from stored fat is not considered. The glucose equivalent of insulin is uncertain. The use of two grams per unit is admittedly arbitrary but nevertheless, it permits comparison within the group.

We may classify 17 cases with negative tolerance as severe, 68 cases with tolerance from 0 to 50 grams as moderate and 104 cases with tolerance exceeding 50 grams as mild. The difficulty with any such classification is that it represents the condition at a given time but not necessarily permanently. Thus, Case 344, had a tolerance of minus 65 grams on November 12-13, 1911, which changed gradually to plus 60 on April 7, 1912. During this period, pulmonary tuberculosis steadily advanced. Rabuchin[9] mentions a case with extensive tuberculosis, in which shortly before death, the urine suddenly became sugar-free although previously hyperglycemia and acetonuria and glycosuria had been excessive. Comparable changes in carbo-

hydrate tolerance in non-tuberculous diabetics also are observed under modern treatment with insulin. In general, it is not low tolerance per se, but the long period of uncontrolled diabetes which is most potent in bringing about the development of tuberculosis.

The concentration of sugar in the urine has not been closely related to the development or course of tuberculosis. Early and young cases of diabetes tend to have the highest percentages. Cases with nephritis and especially cases with sufficient acidosis to interfere with renal function may have relatively small percentages of sugar in the urine when the blood sugar is highest and the prognosis most grave.

b) Blood Sugar. The blood sugar in this series exhibits about the same variations as are found in non-tuberculous diabetes of comparable severity. The blood sugar values were selected at periods at the outset of treatment when the effect of insulin would not enter in and when a period of severe undernutrition or fasting had not immediately preceded the taking of the blood. They were not all fasting specimens, since the administration of insulin during the night would have affected the results in many cases. In three cases the blood sugar was below 0.10 per cent, in 133 cases from 0.10 to 0.30 per cent and in 61 it exceeded 0.30 per cent. High values occur usually in cases with acidosis. Naunyn[10] reported a case with blood sugar over one per cent and in this series there are two cases with a blood sugar over 700 mgs. Case No. 5632, male, had a blood sugar of 0.80 per cent during coma.

A summary of the studies of the blood sugar in non-diabetic tuberculosis is given by Wells and Long[11]. Seitz[12], Rabuchin[9], Langston[13], Landau[14], Berg[15] and McBrayer[16] noted alimentary hyperglycemia in tuberculosis under various conditions.

Borock[17] and Hecht[18] found low sugar values in cases with bad prognosis. Low blood sugar values might be expected when tuberculosis of the miliary or disseminated type had impaired the function of the liver or of the adrenals. Thus, in Case No. 11471 who developed hypoglycemia, at autopsy many tubercles were present in the liver. Fatty livers are found both in diabetes and tuberculosis. The low blood sugar of Addison's disease is well-known. Rabuchin noted the occurrence of many cases of blood sugar below 0.08 per cent fasting in uncomplicated tuberculosis. He held that in advanced exudative processes there was poor glycogen formation. He noted that amylase was increased in the blood in far-advanced cases. He felt that either increased glucose oxidation or possibly defective sugar formation accounted for the low blood sugar values. After 100 grams of glucose the blood sugar in 15 tuberculous cases reached 160 to 180 whereas in normals it only averaged 140 at peak. This was true no matter what the type of process. Also in 42 per cent of 26 cases exudative tuberculosis the plasma CO_2 was below 39 volumes per cent. Experimentally in tuberculous animals he found atrophy and necrosis of the pancreas with shrinking and sclerosis of islands. In one case out of nine diabetic cases with extensive tuberculosis shortly before death the urine became suddenly sugar-free although before hyperglycemia, acetone, sugar two plus showed in all the others.

c) Cholesterol. Cholesterol increases in the blood of diabetic patients inadequately controlled. Some of the highest values are seen in diabetic coma. In a series of 892 diabetics at the Deaconess Hospital the range has been from 65 to 850 milligrams per 100 cc. In tuberculosis, Baemeister and Henes[19] state that the general condition of the patient seems to be the most important factor, for even with a high fever normal or even high cholesterol values may be obtained in the patient if in good condition, low figures being found in cachexia even with fever. Weltman[20] reported that in early tuberculosis normal cholesterol figures may be obtained, but in advanced cases the cholesterol is low, and it falls rapidly in acute active cases, so that he ascribed to the cholesterol figure a prognostic significance in tuberculosis which has been confirmed by later investigations. By a crude comparative method v. Eisler and Laub also found evidence of a cholesterol decrease progressing with the advance of the disease, and measured by the capacity of the free cholesterol to inhibit saponin hemolysis. The decrease concerns chiefly the cholesterol esters.

Blood cholesterol values have been exceptional in a few cases of diabetes with pulmonary tuberculosis at the Deaconess Hospital. In terminal states, as in Case Nos. 2448 and 11471 the cholesterol fell to 78 and 72 milligrams per 100 cc. Variations in cholesterol are indicative of similar variations in the other lipids of the blood, lecithin, fatty acids, and free fat. The relation which these substances bear to infections and to alterations in the diabetic metabolism remains a fascinating problem.

d) Severity of Diabetes. Standards for the measurement of severity are unsatisfactory. One author may consider diabetes severe because of the presence of coma. Another judges the height of the blood sugar or the carbohydrate tolerance. If one remembers the many cases who within a period of months or years change from apparent severity to a condition of such mildness that insulin is reduced or given up, then it is obvious that most adults are fundamentally mild, if the long duration and good general health of modern diabetic children in spite of hyperglycemia and negative carbohydrate balances are considered, even childhood diabetes is mild. The severity of the disease depends chiefly upon the character of its treatment.

Nevertheless, it is true that certain diabetics have become much more emaciated, develop

more severe complications, and require larger amounts of insulin to control glycosuria than do others. Probably the clinical judgment of physicians experienced in diabetic treatment would not vary in classifying such a group. If we classify as severe, cases who have a negative balance after a reasonable period of treatment, 17 such cases are found in this group. Moderately severe cases with a carbohydrate tolerance of 0 to 50 grams number 68, and mild cases with carbohydrate tolerance exceeding 50 grams number 104.

Another grouping may be made on the basis of the amount of insulin used. Thus mild cases would take up to 20 units a day, moderate from 20 to 50 units and severe cases from 50 units upward. In this series but 16 cases were discharged taking over 50 units daily. Of these 16 cases, 11 would have been classified as severe by other methods.

The more severe diabetics are usually the cases who have had coma, have lost much weight and frequently have had a more tardy diagnosis of tuberculosis. These facts must be considered in attempting to ascribe to the severity of the diabetes responsibility for the acute, extensive exudative processes such as bronchopneumonia with caseation and excavation so often reported especially in European literature. Rosenberg and Wolff[21] consider that the severe diabetics tend to develop exudative types of tuberculosis whereas the milder cases tend to the cirrhotic form. Out of 27 cases with exudative types of pulmonary tuberculosis, only six had mild diabetes and 17 were severe. In the cirrhotic forms of tuberculosis mild diabetes occurred in 10 as compared with three of moderate severity. This idea is only partially borne out in our series. Case 4232, female, aged 18, carbohydrate tolerance minus 50 because of constant dietary infractions, developed an exudative process in the right lower lobe with cavitation and later in the left lower lobe, but after two years sanitarium treatment healed the cavity. (See figs. 6, 7 and 8.) Case Nos. 3325 and 4082 with carbohydrate tolerance of minus 26 and minus 29 grams respectively developed chronic ulcerative tuberculosis. The severity of the diabetes appears of marked degree during a highly toxic period of the tuberculosis. Grote[22] considers that there is nothing typical in the form of tuberculosis found in adult diabetics.

e) Diabetic Metabolism before the Development of Tuberculosis. Although the anatomic forms assumed by tuberculosis in diabetes are sufficiently varied to render difficult the selection of typical processes, yet the frequency of its occurrence indicates that some features in the diabetic metabolism must favor the growth of the organism. In table 3 are shown metabolic data of a group of diabetics of varying ages who later developed pulmonary tuberculosis. The data for the first five are taken from Joslin's monograph Diabetic Metabolism with High

TABLE 3

DIABETIC METABOLISM PRIOR TO DEVELOPMENT OF PULMONARY TUBERCULOSIS

Case No.	Sex and Age	Duration of D. M. Yrs.	Age at Onset of Tbc.	Date of Metabolism	Weight Net Kg.	Respiratory Quotient	Heat Output per 24 Hrs. Total	Heat Output per 24 Hrs. Per Kilogram Weight	Total Calories Per cent + or — Standard (H and B)	NH_3	Diacetic Acid	Urinary Nitrogen	Urinary Sugar per 24 Hrs. Gm.	Death Date	Death Cause
177	M 56	8.5	76	IV, 1909	83	0.78	1771	21	+5	—	0	16.4	6	V, 1929	Coronary Thrombosis and Tbc.
220	M 49	8.3		XI, 1908	48	0.70	1598	33	+27	3.3	+	15.3	67	VIII, 1910	Coma
344	M 48	7.5	48	V, 1911	55	0.72	1829	33	+30	5.3	++	13.2	158	IV, 1912	Tbc.
810	M 28	0.3	28	XII, 1914	45	0.76	1238	28	—6	1.3	+	9.3	6	VIII, 1917	Tbc.
1029	M 37	3.8	37	IV, 1916	51	0.80	1123	22	—19	—	0	—	0	I, 1917	Tbc.
1233	M 27	1.2	28	I, 1917	50	0.74	1028	21	—28	—	0	10.7	13	VI, 1918	Tbc.
2448	M 20	2.0	23	X, 1922	47	0.78	1243	26	—15	1.6	++	13.3	82	II, 1928	Tbc.
2687	F 26	2.0	30	XII, 1922	42	0.83	1240		—27	—	+	—	—	IV, 1928	Tbc.

and Low Diets[23] and the last two from his Treatment of Diabetes Mellitus. In the first monograph the data of metabolic experiments with 113 diabetic patients are given and from these I have extracted the data upon those who later developed pulmonary tuberculosis.

Case No. 177 had no evidences of tuberculosis until shortly before his death, 20 years after the metabolism tests. Case Nos. 220, 344, 810, 1029 and 1233 developed tuberculosis within a few months after the metabolism studies here given, and perhaps earlier, although fever and cough were absent during these tests. In Case No. 2448 active tuberculosis was undoubtedly present within a few months after the metabolism studies, but in Case 2687 its course was pneumonic probably developing five years afterward.

This group shows the sharp contrast in basal metabolism between cases treated before June, 1914 and later. This date marked the inauguration of the Allen treatment of undernutrition. The average of 12 basal metabolism determinations before that time was 14 per cent above the normal standard (Harris and Benedict) whereas 11 determinations later were 20 per cent below standard. These differences probably are to be explained entirely by the high caloric feeding in the older period and lower diets in the later. Barbour[24] found a normal metabolism in three cases of tuberculosis and Kocher[25] reported normal figures in a series of 15 afebrile cases at the Trudeau Sanatorium. Grafe[26], however, found an increase in metabolism of 20 to 36 per cent in 7 out of 10 non-febrile cases and even greater increases with fever.

The effect of the high protein content of the older diets is seen in metabolic data of the cases studied before 1914. Although one 24 hour figure of 5.6 grams appears, 5 varied from 15.2 to 22.0 grams. The daily nitrogen excretion per kilogram body weight in cases later developing tuberculosis treated before 1914 was 240.5 milligrams. The average urinary nitrogen based upon 37 patients for 458 days was 265 milligrams. After 1914 the average excretion for three cases later developing tuberculosis was 212 milligrams as compared with 185 for the entire group. The variation from the average is too slight to be of much significance. Extraordinarily high excretion of urinary nitrogen occurs during periods of great loss of weight with untreated diabetes and acidosis. The possibility that the amino acids liberated at such periods provide excessive nutrient material and so favor the development of tuberculosis has been mentioned. Under adequate insulin and dietary treatment nitrogen retention and gain in weight will occur except in cases of toxic advancing tuberculosis.

The average respiratory quotient before 1914 was 0.73 and after 1914 it was 0.78. These figures are almost identical with the averages of 0.73 and 0.77 for the larger groups of non-tuberculous diabetics.

Acidosis of moderate degree was present in three cases, two of which were severe diabetics, as shown by negative carbohydrate balances varying from —5 to —65 grams. Again relation of acidosis and coma to the later development of pulmonary tuberculosis stands out.

That six out of 113 diabetics studied should have developed tuberculosis shows again the high incidence of this complication. All six were males. Three belonged in the pre-Allen era of overnutrition, but one of these, Case No. 177, did not develop tuberculosis until 20 years later. Three belong in the Allen era following June, 1914. The importance of the duration of diabetes in estimating the incidence of tuberculosis also is indicated by the fact that the average duration of life in these six cases was 9.6 years although the average duration of life in 88 out of the original 113 cases who had died by June 1, 1921 was but 4.6 years. This comparison brings out the point that the occurrence of coma prepares the field and recovery from coma with prolongation of life affords opportunity for pulmonary tuberculosis.

3) Clinical Course of Tuberculosis in Diabetics

The development of pulmonary tuberculosis has long been described as exceptionally insidious and difficult of diagnosis in a diabetic. With regard to tuberculosis in general, the concept that pulmonary tuberculosis (not merely the primary tuberculous infection) begins early in life, usually before the twentieth year and pursues a chronic course with periods of relapse and improvement has been gradually gaining acceptance. Cases of so-called acute tuberculosis in late life in a person without previous pulmonary tuberculosis are extremely rare. Among diabetics the acute tuberculous pneumonias, with rapid caseation and cavitation, have been regarded as typical, but the large number of chronic cases pursuing a slow course has been insufficiently stressed, largely owing to the fact that diagnosis of tuberculosis in diabetics has usually been so tardy. Yet in 1913 Magnus-Levy[27], in describing the frequency of tuberculosis in diabetics, wrote that, contrary to the general idea, it often pursued a latent and slow course. Fishberg regards the tuberculosis seen in diabetics as differing in no way from that in non-diabetics. The idea that diabetes in some magic fashion concealed the usual evidences of tuberculosis is based on the tragic discovery which comes occasionally to everyone who sees many diabetic patients that unsuspected advanced pulmonary tuberculosis is the real cause for an unexplained downward course. When the histories of a considerable number of cases

are analyzed, chronicity rather than acuteness is the prevailing characteristic.

The onset of tuberculosis is difficult to establish. The onset of symptoms of loss of weight, emaciation, cough, purulent sputum, night sweats in this series usually meant that the lesion not only was far advanced in a structural sense but that the toxic effect was also advanced. Case No. 7486, whose x-ray in 1930 at the age of 28 years showed merely scarring at the apices and calcification of the tracheobronchial glands, when tuberculosis was found to be advanced in 1932, at first denied any symptoms preceding two months before. Yet on repeated questioning we found that at the age of 19 for two consecutive winters he had bronchitis all during the winter and was incapacitated much of the time. Again three years before the present breakdown he had so-called bronchitis all winter. There can be little doubt that his tuberculosis had been active more than once for considerable periods before the final attack. Naturally the problem of the effect exerted by his diabetes in bringing on the present attack remains. The course of tuberculosis in the non-diabetic has always been known to be insidious and its development to an advanced stage without demonstrable physical signs has occasioned no surprise. In fact those writers who have ascribed to the development of tuberculosis in diabetics a peculiarly insidious quality have never cited figures which would give the facts upon which any special conclusion could be based. Most statements have been made on the basis of comparatively small series of cases. One must not forget the insidiousness of its development in diabetic and non-diabetic alike.

The type of onset of tuberculosis varies in the diabetic as in the non-diabetic. Hemoptysis has been regarded as rare in diabetics, but it is recorded in 45 of the 246 cases in this series or 18 per cent. However, hemoptysis was not always the initial symptom, and it must not be inferred that in 18 per cent of this series the onset was hemorrhagic. Pleurisy with effusion is uncommon. The most frequent types of onset are catarrhal, bronchitic and insidious. Repeated head colds with sputum which the patient describes as catarrh, attacks of bronchitis, or "grippe" without prompt recovery, unexplained fatigue and loss of weight and appetite without a slight fever are common. Repeatedly a patient denies having a cough yet during the office examination demonstrates a loose and productive cough, which by reason of its chronicity he either has forgotten or has labelled "clearing my throat". The insidiousness of the onset in diabetes may well be compared with non-diabetic tuberculosis as exemplified by a series from Trudeau Sanatorium analyzed by Lawrason Brown[28].

Among 1900 consecutive cases admitted to the institution between July, 1920 and April, 1927, there were 503 who presented upon physical examination no changes characteristic of tuberculosis. A number gave a history of pleurisy with effusion in the past and had abnormal physical signs at the bases without râles. All had x-ray evidence of tuberculosis; 159 were in the minimal, 322 in the moderate, and 22 in the far-advanced stage. Of the group 59 per cent had tubercle bacilli in the sputum while under observation and practically all as a result of follow-up were proved to have pulmonary tuberculosis. More than 25 per cent of the entire series of 1900 cases therefore had pulmonary tuberculosis without characteristic physical signs. No one has yet reported a series of diabetics with proved pulmonary tuberculosis in which so high a percentage had no physical signs. Nothing stimulates care in making routine examinations of the lungs of diabetics so much as a review of 245 cases with the discovery that one's own notes record no physical signs on one day and abundant signs a few days later. Banyai[29] mentions three factors which may tend to cause an absence of symptoms in early diabetic tuberculosis: 1) localization in or about the hilum, 2) suppression of allergy and allergic responses by acidosis, 3) age. In older individuals the lymphatics are less permeable and the bacilli may thus spread less easily. The glands are fibrosed and more resistant to tuberculosis. Furthermore, in age there is less tendency to exudative, inflammatory and febrile processes. The sputum was positive in 27 of his 31 cases. On the other hand, Fitz states that although it had been his impression that pulmonary tuberculosis may be difficult to recognize in a diabetic, examination of the clinical records for physical signs indicated that regardless of how the process began, most of the cases developed in a short time the common signs of pulmonary tuberculosis, and tubercle bacilli, if carefully searched for, could be found in the sputum.

Among 245 cases it has only been possible to find 10 whose histories included none of the following symptoms, cough, sputum, hemoptysis, pleurisy with effusion, fever or night sweats. In six of these, observation for a few days only without a sufficiently prolonged follow-up may have been mistaken in interpreting as active what was really a healed or healing process. In four of the ten cases with minimal lesions, no symptoms or signs were found. In others the observation during a terminal complication, such as coronary thrombosis, pneumonia, and most important of all, I believe, errors or deficiencies in histories are responsible. No good evidence has ever been presented to show that in a considerable diabetic series tuberculosis develops with fewer symptoms or physical signs than in non-diabetics.

The fact that so few cases are found without physical signs shows clearly how tardy has been the diagnosis. In only 10 out of 89 cases (see table 7) could the pulmonary lesion be called minimal. It is true that I have not included in this series 58 cases who in a series of routine x-rays are classified as "suspicious". Opinion might be divided, and the inclusion of some as showing definite parenchymal change would raise the percentage.

In this series with the utmost conservatism 38 cases have been found in whom there can be no doubt whatever that active pulmonary tuberculosis began before the onset of diabetes. Leitner's[30] case had tuberculosis 12 years before diabetes. Wassmund[31] had 14 cases, in one of which the tuberculosis preceded diabetes by four years. Ritter[32] mentions a case observed in the tuberculosis ward of the Jackson Memorial Hospital and summarizes other statistics in this point. Brown (quoted by Ritter) mentions a case in which diabetes clearly developed in a patient with pulmonary tuberculosis. It is true that patients who are underweight rarely develop diabetes and for this reason development of diabetes in a person who has active pulmonary tuberculosis would be comparatively infrequent, but I am sure that a more careful analysis of the histories together with more frequent examination of the lungs by x-ray would clearly show that diabetes does develop frequently in the tuberculous.

X-Ray Examinations

a) The results of x-ray examinations of 1659 consecutive diabetic patients unselected except that they were admitted to the New England Deaconess Hospital for treatment of diabetes between 1927 and 1930 and in addition roentgenograms of an earlier period are available for study. With the coöperation of Dr. Gerald Webb, Dr. L. B. Morrison and Dr. Isabel K. Bogan, a series of 341 diabetic patients, originally non-tuberculous, have had roentgenograms at intervals of three to six months in order to observe the earliest lesions of pulmonary tuberculosis, should it develop. The first film of each one has been included in the total of 1659 cases first mentioned. In tables 4 and 5 these films have been classified by sex, by the decade of age and by the duration of the diabetes.

Although males formed only 43 per cent of the entire series 75 per cent of the cases of acute and chronic pulmonary tuberculosis were males. On the other hand, calcified tracheobronchial glands occurred with equal frequency in the two sexes. Thus one may conclude that although both sexes were equally infected early in life male diabetics are almost twice as likely to break down with pulmonary tuberculosis as are females.

The distribution of pulmonary tuberculosis by decade of age shows 15 cases or 37 per cent

TABLE 4

X-Rays of Lungs of 1659 Consecutive Diabetics According to Age of Patients

Age Years	Class (See foot notes) 1	2	3	4	5	6	7	Total
Males								
0-9	13	9	20	3		1		46
10-19	6	8	72	10	1			97
20-29	8	2	47	5	1			63
30-39	10	4	67	3	4			88
40-49	16	3	61	2	5			87
50-59	11	7	112	2	7			139
60+	15	6	167		10			198
Females								
0-9	11	8	16	4				39
10-19	9	4	77	14				104
20-29	2	3	50	6	1			62
30-39	6	3	58					67
40-49	17	5	94	1	1			118
50-59	35	13	203	5	4			260
60+	28	10	245	3	5			291

Note: Key to Column Headings.

1=Normal.
2=Tracheobronchial adenitis; i.e. visible glands.
3=Tracheobronchial adenitis with calcification.
4=Doubtful or "suspicious" pulmonary tuberculosis.
5=Chronic pulmonary tuberculosis.
6=Acute pulmonary tuberculosis. Softly cloudy, homogeneous infiltration. No evidence of previous tuberculous infection.
7=Old healed pulmonary tuberculosis. Fibrous strands in apex and sub-clavicular areas with small calcified areas in the parenchyma. Twenty-one cases in this group are included under heading 3 because of the presence of calcified tracheobronchial glands.

TABLE 5

X-Rays of Lungs of 1659 Consecutive Diabetics According to Duration of Diabetes

Duration Years	Class (see foot note) 1	2	3	4	5	6	7	Total
Males								
0-1	28	11	138	5	9			191
1-4	30	18	202	13	7	1		271
5-9	12	5	121	6	5			149
10-14	3	3	48	1	2			57
15-19	4	1	24		2			31
20+	2	1	13		3			19
Females								
0-1	24	15	189	7	2			237
1-4	46	14	248	14	5			327
5-9	20	12	204	11	2			249
10-14	11	2	55	1	2			71
15-19	3	2	31					36
20+	4	1	16					21

Note: Key to Column Headings.

1=Normal.
2=Tracheobronchial adenitis; i.e. visible glands.
3=Tracheobronchial adenitis with calcification.
4=Doubtful or "suspicious" pulmonary tuberculosis.
5=Chronic pulmonary tuberculosis.
6=Acute pulmonary tuberculosis. Softly cloudy, homogeneous infiltration. No evidence of previous tuberculous infection.
7=Old healed pulmonary tuberculosis. Fibrous strands in apex and sub-clavicular areas with small calcified areas in the parenchyma. Twenty-one cases in this group are included under heading 3 because of the presence of calcified tracheobronchial glands.

in the sixth decade and 11 or 27 per cent in the seventh decade. Thus 64 per cent of the cases of tuberculosis were over 50 years of age, although only 53.5 per cent of the entire series were in this age group.

The influence of duration of diabetes is well shown in spite of the fact that such a series contains a proportionately small number with diabetes of long duration. Four hundred and twenty-eight cases, or 25 per cent, had had diabetes less than one year. The fact that among these were 11 cases of chronic pulmonary tuberculosis indicates the development of diabetes in patients some of whom probably had already had tuberculosis. One thousand and twenty-six cases, or 62 per cent of the entire group, had had diabetes less than five years. A total of 24 cases or 60 per cent of the total number of pulmonary tuberculosis occurred in this group. With diabetes of longer duration the incidence of tuberculosis definitely increases. Thus 235 cases or 14 per cent of the 1659 had diabetes of more than 10 years' duration and in this group are found nine cases of pulmonary tuberculosis or 22.5 per cent of the total number of tuberculous cases. If males alone are considered it will be noted that among 50 cases with duration of diabetes exceeding 15 years, there were five cases of tuberculosis, or 10 per cent. When the duration exceeded 20 years three out of 19 or 16 per cent had tuberculosis.

Fifty-eight cases were classified as "suspicious" under class 4. In two instances follow-up films have shown pulmonary tuberculosis, which in one case went on to tuberculous pneumonia with cavitation.

b) *Interpretation of Roentgenograms in 87 Diabetics with Pulmonary Tuberculosis.* In table 6 is given an analysis of roentgenograms reviewed with Dr. L. B. Morrison and Dr. I. K. Bogan with special reference to evidences of old infection, the extent and character of the processes. No attempt will be made to define the standards of interpretation other than to describe certain typical films and to reproduce others as illustrations.

Primary lesions. In childhood the primary lesion is a small nodule of caseous necrosis that usually becomes calcified. It is usually subpleural and may easily be obscured by overlying ribs, heart or diaphragm. Such lesions may be multiple. They are recognizable when from 0.2 cm. to 1 cm. in diameter and may be simulated by vessels radiating so as to be seen "on end." When as large as 0.5 cm. they usually suggest a heavy infection in childhood. Such large primary lesions are recognizable in 12 of this series, but smaller areas of calcification in the parenchyma are found in practically all cases. Naturally many such large primary lesions are not recognized in cases of chronic pulmonary tuberculosis because of fibrosis and later calcification.

Hilum Tuberculosis, or tuberculosis of the tracheobronchial nodes. As a result of the primary focus of infection, the lymph glands lying along the path of lymphatic drainage are involved. These nodes lying for the most part in the angles formed by the branches from the main bronchi are of the same density as the structures surrounding. Furthermore, even if somewhat enlarged, they often lie among blood vessels which break up the shadows cast by their boundaries. Hence unless calcified, these glands involved by caseation are not visible until greatly enlarged. Among the 1659 consecutive films visible tracheobronchial glands uncalcified were noted 85 times. In the 87 cases of pulmonary tuberculosis, uncalcified glands were seen in 32 cases, but in all these with four exceptions, calcified glands were also present. The presence of four cases of non-calcified tuberculous nodes associated with pulmonary tuberculosis would suggest the possibility of a primary process in the lungs like that of childhood. In one, a physician, 60 years of age, miliary tuberculosis was present. In the other three, small areas of calcification in the parenchymal indicated old healed infection. It is more likely that some calcification existed in the tracheobronchial glands but was not visible because of anatomical peculiarity or slight blurring.

Calcified tracheobronchial glands were recognized in 64 out of the 87 cases. These shadows lying lateral to the bronchi along the main arteries are usually well recorded even if calcification is not heavy, provided exposures are rapid enough to prevent blurring. The shadows are granular, or crenated and irregular in outline. When rounded and dense they may resemble an artery seen on end.

Such calcification was observed in 42 per cent of 85 diabetic children under 10 years of age and in 74 per cent of 201 diabetic children from 10 to 20 years of age. No such frequency has been found in unselected non-diabetic groups of comparable age. In Massachusetts school children chest x-rays were done only in cases with positive tuberculin tests and the incidence of the childhood type, usually with calcified glands was but two per cent. Altschul[33] considers calcification rare in the hilus of the child. McPhedran[34] regards tracheobronchial calcification as an evidence of severe infection in children, usually occurring in contact cases. The infection may have occurred in childhood and ceased or it may have continued. It is not to be dismissed lightly in a diabetic child certainly for already from this group have come five cases of pulmonary tuberculosis developing during the second decade.

Multiple areas of calcification in the parenchyma. In 69 cases of the 89 multiple small areas of calcification were recorded, usually on both sides. In eight only single areas appeared. These clearly must represent repeated infections in many instances in childhood. The number

TABLE 6

Summary of Chest Roentgenograms of 8

Case No.	Age Yrs.	X-Ray Findings: Parenchyma: Infiltration	Parenchyma: Fibrosis	Parenchyma: Calcification	Hilum: Glands	Hilum: Calcification R.	Hilum: Calcification L.	
Male								
4765	25	R. 1 to 4	R. 1 to 2	++	+			
9354	43	L. 1 to 5	R. 1 to 2	0	0	+		
8116	51	L. 1 to 2	L. 1 to 2	++	+	+		
5434	38	L. 1 to 3	L. 1 to 6	+	0	+	+	
5932	19	L. 6 to 9	L. 6 to 8	+++++	0	+	+	
5719	25	L. 1 to 6	R. to 1, L. 1 to 6	++++	+	+	+	
5682	65	L. 6 to 8	R. to 1, L. 1 to 3	0	+	+		
8089	44	R. 6 to 8, L. 6 to 9	L. to 6	+++	0	+	+	
968	56	R. 1 to 7, L. 1 to 3	R. 1 to 7, L. 1 to 3	0	0	+	+	
7186	51	R. 1 to 6, L. 1 to 4	R. 1 to 6	+++	0			
7793	67	R. 3 to 7, L. 4 to 5	R. 3 to 7, L. 3 to 5	+++	0	+		
1642	60	L. 1 to 8	L. 1 to 2, R. 1 to 3	++++	0	+	+	
4961	77		R. 1 to 7	+++	0	+		
6053	60	R. 4 to 7, L. 4 to 7	R. 4 to 7, L. 2 to 5	++++	+	+		
6669	52	L. 1 to 5, R. 1 to 4	R. 1 to 4	++++	0	+	+	
4832	32	R. 1 to 8, L. 1 to 8	L. to 7, R. to 7	++++	0	+		
177	73	L. 1 to 6	L. to 6	++++	0	+		L
9213	52	R. 6 to 8	R. 6 to 8	+++++	0	+	+	
8375	37	R. 6 to 7	R. 2 to 6, L. 2 to 6	+++++	0			
8314	72	R. 6 to 9	R. 6 to 8	++++	0	+		R
4624	36	R. 4 to 6, L. 3 to 5	R. 4 to 6, L. 3 to 5	+++	0			L
4837	53	R. 4 to 8	R. 4 to 8	+++	0			
8737	50	R. 1 to 9	R. 1 to 9	+++++	0	+	+	
7134	36	L. 7 to 10	L. 7 to 10	++++	0			L
3141	61	R. 6 to 7, L. 6 to 8	R. 1 to 7, L. 1 to 8	+++++	0	+	+	L
10503	44	L. 3 to 5	L. 3 to 5	+++++	0	+	+	L
10622	51	R. 7 to 11	R. 7 to 11	++++	0	+	+	R
3209	64	R. 3 to 6	R. 1 to 7	+++++	0	+	+	
9338	32	R. 7 to 11	R. 7 to 11	+++++	0	+	+	
2274	14	R. to 5, L. to 9	R. to 5, L. to 9	+++	+	+	+	L
6627	21	R. 1 to 7, L. 6 to 7	R. 1 to 7, L. 6 to 7	++	+	+		R
4045	61	Miliary throughout		++	+			
2448	24	R. to 8, L. to 6	R. to 8, L. to 6	++	0			L
7553	59	R. 1 to 7, L. 1 to 6	R. 1 to 7, L. 1 to 6	+	+			
6809	33	R. 3 to 7, L. 1 to 6	R. 1 to 7	++++	+	+		R
6184	55	R. 1 to 10, L. 1 to 7	R. 1 to 10, L. 1 to 7	+++++	0			L
5716	69	R. 1 to 7, L. 1 to 7	L. 1 to 7					L
6725	54	L. 1 to 8, R. 1 to 6	R. 1 to 7, L. 1 to 8	+++	0	+		L
629	81	L. 2 to 7	R. 1 to 7, L. 1 to 7	+++++	+			L
2273	56	R. 2 to 9, L. 3 to 7	R. 2 to 9	++	+	+		R
9661	62	R. 1 to 6, L. 4 to 8	R. 1 to 6, L. 4 to 8	+++	0			R
7450	39	R. 2 to 7, L. 2 to 5	R. 2 to 7, L. 2 to 5	+++++	0	+	+	R
6702	65	R. 6 to 8, L. 4 to 8	R. 6 to 8, L. 4 to 8	+++++	0	+		L
8239	52	R. 1 to 9, L. 1 to 6	R. 1 to 9, L. 1 to 6	+++	0			L
7621	65	R. 1 to 8, L. 8 to 10	R. 1 to 8, L. 3 to 8	+++++	0			
2164	70	L. 5 to 9	R. 1 to 9, L. 1 to 9	+++++	0			R
10228	41	R. 4 to 10	R. 4 to 10, L. 3 to 9	++	0			R
7330	79	R. 7 to 10, L. 1 to 8	R. 1 to 10, L. 1 to 9	+++++	0	+	+	R
11023	34	R. 1 to 7, L. 1 to 8	R. 1 to 7, L. 1 to 8	+++++	0	+	+	R
9821	58	R. 1 to 8, L. 1 to 8	R. 6 to 8, L. 1 to 8	+++++	0	+		
10303	54	R. 6 to 8, L. 1 to 11	R. 6 to 8, L. 1 to 11	+++++	0			L
8722	43	R. 4 to 7, L. 1 to 8	R. 4 to 7, L. 1 to 8	+++++	0	+	+	R
7041	15	R. 5 to 8, L. 5 to 9	R. 5 to 8, L. 5 to 9	0	0			R
6791	42	R. 4 to 10, L. 2 to 10	R. 1 to 11, L. 1 to 12	0	0			
7486	36	L. 1 to 9	L. 1 to 9	+++	0	+	+	L
1871	55	L. to 6, R. to 3	L. 1 to 6	++++	+	+	+	L
Females								

Cavities		Apices	Grade	Notes
Location	Size Cm.			
		R. and L. fibrosed	Min.	
		L. fibrosed	Min.	
		L. calc.	Min.	
		Caps thickened	Min.	
			Min.	
		R. and L. fibrosis	Mod.	
		L. fibrosed	Mod.	
			Mod.	
		R. fibrosed	Mod.	
		R. and L. fibrosed	Mod.	
			Mod.	
			Mod.	
		R. fibrosed	Mod.	
		L. fibrosed	Mod.	
		R. and L. fibrosed	Mod.	
		R. and L. fibrosed	Mod.	
L. 1	4	R. and L. fibrosed	Mod.	
			Mod.	
		R. and L. fibrosed	Mod.	
R. 1	4		Mod.	
L. 1	3		Mod.	
			Mod.	
		R. infiltration	Mod.	
L. 1	3		Mod.	
L. 1	3	R. and L. fibrosed	Mod.	
L. 1	2	L. fibrosed	Mod.	
R. 1	3.5		Mod.	
		R. fibrosed	Mod.	
			Mod.	
L. 1 and 2	4	R. fibrosed, L. haze	Far	Left collapse
R. 1	2	L. and R. fibrosed	Far	
			Far	
L. 1	3.5	R. fibrosed	Far	Calc. R. cerv. glands
		R. and L. fibrosed	Far	
R. 1 and 2 (3)	4.5		Far	
L. 1	10	R. dense cap	Far	
L. 1	4	R. fibrosed	Far	
L. 1 and 2	5	R. and L. fibrosed	Far	
L. 1	5	R. dense cap, L. fibrosed	Far	
R. 2	4	R. fibrosed	Far	
R. 1, L. 1	4	R. and L. fibrosed	Far	
R. 1, L. 1	4	R. and L. fibrosed	Far	
L. 1	3	L. fibrosed	Far	
L. 1 and R. 2	5	L. fibrosed	Far	
		L. and R. fibrosed	Far	
R. 1 and L. 1	5	R. and L. fibrosed	Far	
R. 1 and 2 multiple	6		Far	
R. 1, L. 1	8		Far	
R. 1	2	R. and L. infiltration	Far	
		R. and L. fibrosed	Far	
L. 1	1	L. fibrosed	Far	
R. 1	2.5	L. fibrosed	Far	
R. 2, L. 2	6		Far	Pneumothorax both apices
		R. and L. fibrosed	Far	
L. 1	7.5	L. dense pleura	Far	
L. 1	5	R. and L. fibrosed	Far	
		Caps thickened	Min.	

7330	79	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
11023	34	R. 1 to 7, L. 1 to 8	R. 1 to 7, L. 1 to 8	+++++	0	+ +	R. 1
9821	58	R. 1 to 8, L. 1 to 8	R. 6 to 8, L. 1 to 8	+++++	0	+	
10303	54	R. 6 to 8, L. 1 to 11	R. 6 to 8, L. 1 to 11	+++++	0		L. 1
8722	43	R. 4 to 7, L. 1 to 8	R. 4 to 7, L. 1 to 8	+++++	0	+ +	R. 1
7041	15	R. 5 to 8, L. 5 to 9	R. 5 to 8, L. 5 to 9	0	0		R. 2,
6791	42	R. 4 to 10, L. 2 to 10	R. 1 to 11, L. 1 to 12	0	0		
7486	36	L. 1 to 9	L. 1 to 9	+++	0	+ +	L. 1
1871	55	L. to 6, R. to 3	L. 1 to 6	++++	+	+ +	L. 1
Females							
4945	53	L. 3 to 4	R. 1 to 3, L. 1 to 5	+	+	+	
7263	28	R. 1 to 2	R. to 2	0	0	+ +	
6287	47	R. 4 to 5	R. 4 to 5	+	0	+	
11006	19	R. 8 to 10		+++++	0	+ +	
6205	50	R. 1 to 6	R. 1 to 6	(Motion)	+		
5571	78	R. 1 to 7	R. 1 to 7	0	+		R. 1
7255	39	L. 2 to 7 (½ lung)	R. 1 to 8, L. 1 to 7	++++++	+	+	
7195	56	R. 3 to 5, L. 3 to 5	R. 3 to 5, L. 3 to 5	0	+	+	R. 1 (3
7603	27	R. 3 to 4, L. 3 to 5	R. 3 to 4, L. 3 to 5	(Motion)	+	+	R. 1
9270	63	R. 1 to 4, L. 1 to 2	R. 1 to 4, L. 1 to 3	+++	+	+	
9151	45	R. 1 to 5, L. 1 to 5	R. 1 to 5, L. 1 to 5	++++	+	+	
7757	54	R. 1 to 5, L. 1 to 6	L. 1 to 6	++++	+	+	
6646	46	R. 1 to 6	R. 1 to 6	+++	+	+ +	
10163	29	L. collapse	L. 1 to 6	++++	0	+	
7608	70	R. 3 to 5, L. 4 to 6	R. 3 to 5, L. 3 to 5	++++	+	+ +	
4763	23	R. 7 to base	R. 1 to 7	+++++	0	+	R. 2
4082	58	R. 3 to 7	R. 3 to 7, L. 6 to 8	++	0	+	R. 1
7238	62	R. 1 to 8, L. 3 to 5	R. 1 to 8, L. 3 to 5	+++++	0	+	L. 1
4232	20	R. 7 to 9, L. 4 to 8	R. 7 to 9, L. 4 to 8	++	0	+	R. 3
11214	53	L. 4 to 8	L. 4 to 8	+++++	0	+ +	
8435	44	R. 3 to 6	R. 1 to 4	+++	0	+ +	
6139	64	R. collapse, L. 6 to 9 R. 1 to 6, R. 7 to 9	R. 1 to 6, L. 5 to 9	0	+	+ +	R. 1
5659	35	R. 6 to 10, L. 6 to 8	L. 3 to 8	+	0		R. 2
7437	77	R. 3 to 8	R. 3 to 8	+++++	+	+ +	R. 1 (
5375	58	R. 3 to 7, L. 3 to 7	R. 3 to 7, L. 3 to 7	++	0		R. 1
7143	50	R. 3 to 6, L. apex to base	R. 2 to 6, L. 1 to base	+	0		L. 1
3325	43	R. 2 to 6, L. 2 to 6	R. 2 to 6, L. 2 to 6	+	+		
5270	62	R. 6 to 9, L. 2 to 4	R. 6 to 9, L. 2 to 4	+	+	+ +	L. 1
7876	71	R. 5 to 7, L. 4 to 10	R. 5 to 7, L. 4 to 10	+++	0		
5917	63	R. 1 to 10	R. 1 to 10, L. 1 to 6	0	0		
5976	72	R. 2 to 4, L. 1 to 9	R. 2 to 4, L. 1 to 9	0	0	+ +	

KEY TO HEADINGS

1) Infiltration includes haze, mottling and consolidation. The exte
of ribs posteriorly, but the lateral borders are not recorded.
mottling from top of lung to top of 4th rib. Sputum positiv
2) Fibrosis in dense, strand-like markings, also recorded accordi
3) Calcification includes small areas, which are recorded from +
presence in from one to five lobes.
4) Hilum glands are recorded as merely visible or as calcified.
5) Cavities are localized according to lobe. Thus R. 1 and 2 mean
lobes.
6) Apices include the area above the clavicle only.

R. 1	2	R. and L. infiltration	Far	
		R. and L. fibrosed	Far	
L. 1	1	L. fibrosed	Far	
R. 1	2.5	L. fibrosed	Far	
R. 2, L. 2	6		Far	Pneumothorax both apices
		R. and L. fibrosed	Far	
L. 1	7.5	L. dense pleura	Far	
L. 1	5	R. and L. fibrosed	Far	
		Caps thickened	Min.	
		R. fibrosed	Min.	
			Min.	
			Min.	
			Mod.	
R. 1 multiple	1	R. fibrosed	Mod.	
		Caps thickened	Mod.	
R. 1 (3)	1.7	R. and L. fibrosed	Mod.	
R. 1	1	R. fibrosed	Mod.	
		L. fibrosed	Mod.	
		R. haze, L. fibrosed	Mod.	
		R. fibrosed, L. calc.	Mod.	
		R. and L. fibrosed	Mod.	
		L. fibrosed	Mod.	
		R. and L. fibrosed	Mod.	
R. 2	2	R. fibrosed	Mod.	
R. 1	2.5	R. fibrosed	Mod.	
L. 1	1.5	R. and L. fibrosed	Mod.	
R. 3	3.5		Mod.	
		R. and L. fibrosed	Mod.	
		R. and L. fibrosed	Mod.	
R. 1	3	R. fibrosed	Far	
R. 2	3	Caps thickened	Far	
R. 1 (2)	3	R. fibrosed	Far	
R. 1	2.5	L. fibrosed	Far	
L. 1	2	R. and L. fibrosed	Far	
		R. and L. fibrosed	Far	
L. 1	3	R. and L. fibrosed	Far	
			Far	
		R. and L. fibrosed	Far	
		R. and L. fibrosed	Far	Partial collapse left lung

gs

The extent is recorded according to the level recorded. Thus Case No. 4765 showed soft m positive.

l according to the level of ribs posteriorly.

l from + to +++++, according to their

lcified.

d 2 means cavities in right upper and middle

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of areas of calcification together with the frequency of exposure and finally the histories usually obtainable of frequent bronchitis and head colds over a period of years indicate clearly that in diabetes also the course has been a long and chronic series of infections, flare-ups and arrests preceding the final development of extensive tuberculosis.

Classification of Progression. The 89 cases may be divided according to the standards of the National Tuberculosis Association into minimal, moderate and far-advanced cases.

(1) Minimal lesions were found in but 10 cases listed in table 7. The rarity of the discovery of active tuberculosis in a minimal stage, judging by the literature justifies reporting these cases in some detail. In all cases calcification of the tracheobronchial glands (8 cases) or small areas of calcification in the parenchyma (10 cases) indicated preëxisting healed or partially healed infection. Case 4945, female, had been treated in a state tuberculosis sanitarium 20 years previously and showed fibrous strands characteristic of old healed tuberculosis at her apices, as well as a fresh minimal lesion.

Case Nos. 4045 and 5434 were physicians, the first, a surgeon, had pleurisy with effusion six months before the examination, and the second was engaged part-time in examination of tuberculous service men for the Army. Case No. 7263 was a nurse employed in a tuberculosis dispensary. The brother of Case No. 6287 had both diabetes and tuberculosis. The origin of tuberculosis in Case No. 5932 was a mystery until it was discovered that a fellow clerk in the grocery store where he was employed had a positive sputum.

Case Nos. 9354 and 11006 had just recovered from diabetic coma when their lesions were discovered. It seems hardly possible that 48 hours of coma could have produced the changes recorded by x-ray, but one must remember that a serious metabolic disorder with acidosis probably precedes by days or weeks the onset of actual coma.

TABLE 7

TEN DIABETIC CASES WITH MINIMAL PULMONARY LESIONS

Case No.	Sex	Age yrs.	Duration Diabetes, yrs.	Symptoms at Time of X-ray	Location* of Lesion	Later Course
7263	F	30.7	4.3	Cold, fever	Hazy infiltration, rt. apex	Sanitarium, Sept. 1932
6287	F	16.8	10.0	None	Infiltration rt. 4 to 5	Sanitarium, Sept. 1932
4765	M	25	0.1	Cough	Fan-shaped area rt. 1 to 4	Living Mar. 1931
4045	M	60	0.5	None	Area infiltration rt. 1 to 2	Died miliary tuberculosis 2 mos. later
9354	M	43	0.5	Coma	Mottling left 1 to 5	State Sanitarium 1932
4945	F	52	2.5	None	Mottling left 1 to 3	Home
8116	M	51	10.0	Cough, sputum	Apical infiltration rt. apex	Living Oct. 1929
5932	M	18.7	5.0	Fever	Infiltration left 6 to 9	Sanitarium Sept. 1932, with process advancing. Arrested Oct. 1933
11006	F	19.4	0.9	Cough, coma	Focal infiltration rt. lower lobe	Home
5434	M	38	1.0	Pigmentation Asthenia	Left Apex hazy infiltration	Died 3 weeks later of Addison's Disease and Myocarditis

*Extent of lesion is measured by ribs posteriorly.

The characteristic features of these early lesions are (1) localization in the apex in all but 3 (Case Nos. 5932, 6287 and 11006), (2) extension of the process below the clavicle in 7, (3) basing of the infiltration, usually although not always cone-shaped, upon the pleura with extension inward toward the hilum, (4) the softness and lack of sharp marginal definition of the shadows. Figure 1 illustrates a lesion at the level of the hilum.

(2) Moderately advanced lesions occurred in 41 and far advanced cases numbered 38. Thus 89 per cent of this series had passed the minimal stage before diagnosis. Progression of pulmonary tuberculosis is often so rapid and the symptoms as well as physical signs so slight that only by frequently repeated films can one hope to discover minimal lesions. Four of these 10 cases were found in this way.

Anatomical extent of the Process. Owing to the advanced stage of most cases in this series, tuberculosis limited to the upper third of the lung does not form a large percentage of the group. In all cases lesions occur below the clavicles. Fibrosis and scarring of the apices are

almost the rule. Mottling, consolidation or cavitation in the upper third of the lung occurred in 73 of the 89 cases, but usually in association with

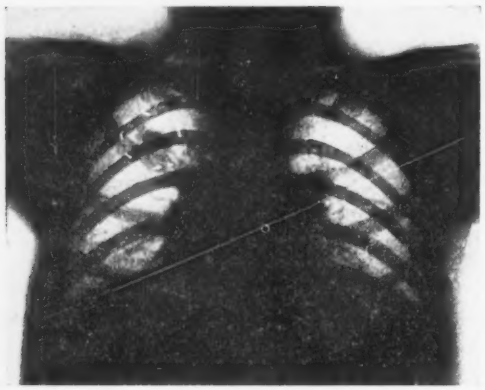

FIG. 1. Case 6287, F. schoolgirl. Aged 16.8 yrs. in June, 1932. Duration of diabetes 10.1 yrs. Repeated attacks of coma. X-ray showed no lesion one year previously. The above lesion cleared after three months in a sanatorium. Living at home August, 1933.

processes in other portions of the lungs. Basal tuberculosis, and active tuberculosis limited to the regions at the level of the hilum, occurred in but 16 cases.

A striking difference appears in this respect if comparison is made with Sosman's[35] findings at the Peter Bent Brigham Hospital. In 45 cases he reported 16 cases of healed apical lesions, eight cases of ordinary "adult" apical lesion and 21 of the "hilum" or unsensitized type. By "hilum" he means not glandular tuberculosis but bronchopneumonic processes at the level or below the level of the hilum, similar in their tendency to progression to the tuberculosis of unsensitized children or races. In commenting upon his findings, J. B. Amberson and R. G. Allison also noted the frequency of such types among diabetics, while F. S. Bissell felt that such types occur with equal frequency among non-diabetics. The question of the existence of a type of lesion peculiar to diabetes turns upon the frequency of bronchopneumonic lesions at the level and below the hilum. Bernard[49] from his great experience in Paris divides the lesions below the clavicle according to three regions a) intercleido-hilar, between the hilum and clavicle, b) parahilar, at the level of the hilum and c), basal. He regards the parahilar lesions as common. The pulmonary changes due to tuberculosis are so variable and bizarre that conclusions based upon small series of diabetics are apt to be misleading. In this series of 89 cases basal tuberculosis as illustrated in figures 2 and 6 forms but a small part of the series. If Sosman's series and this series are combined the total incidence of "hilum" and basal tuberculosis would be no greater than might be found in an equal number of non-diabetic cases of pulmonary tuberculosis.

Course and Rapidity of Extension.

The evidence from areas of calcification in the parenchyma, Ghon tubercles and calcification of the tracheobronchial glands of early infection of diabetics is overwhelming. When the development of adult tuberculosis is to occur seems to be influenced by the factors of repeated infection by contact with open cases and to be favored by the development of diabetes and diabetic acidosis. In this group the earliest lesions are predominantly apical and sub-clavicular although exceptions occur. Certainly apical (including lesions just below the clavicle) tuberculosis of the adult type with or without healing is present in the great majority. Other portions of the lung seem to be involved with varying rapidity and varying sequence. Case No. 4763 illustrates the rapid development of a lobar consolidation of the right lower lobe. See figure 2. In spite of an apparently hopeless outlook

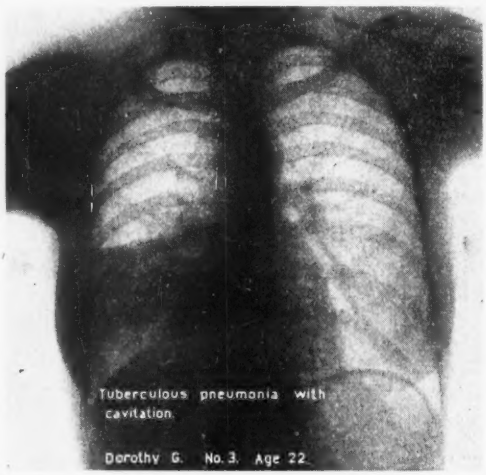

FIG. 2. Case 4763, F., a pupil nurse in December, 1931. Onset of diabetes at 16 years. Rapid development of lobar consolidation of right lower lobe, with cavitation. Positive sputum. Calcified glands in abdomen and at hilum were observed five years previously. Doing well at Rutland State Sanatorium in February, 1933.

in November, 1931, she is greatly improved in July, 1933.

Case No. 5932, after recovery from coma due to a carbuncle continued to have an afternoon temperature of 99° to 100°. Figures 3 and 4 show the extension of his process with dates. Note the involvement of the right apex in the second film. This type of lesion originating at the level of the hilum without antecedent apical process and with the calcified nodes of childhood, often progresses rapidly to excavation. At an x-ray examination in September, 1932, the process had extended to involve a large part of the lower half of the left lung in an exudative consolidation. He spent nearly two years in State and city hospitals. In October, 1933, he weighed 136 pounds, had no cough or sputum, took 80 units of insulin daily.

Rapidly extending bronchopneumonic processes in the perihilar regions are rather rare in this series. McPhedran[36] has stressed the importance of films taken after rotation of the patient in order to make certain that infiltrations

and cavities apparently in the hilum are not really anterior or posterior to it. Many reports of short series have emphasized this type but when a large number are grouped, the

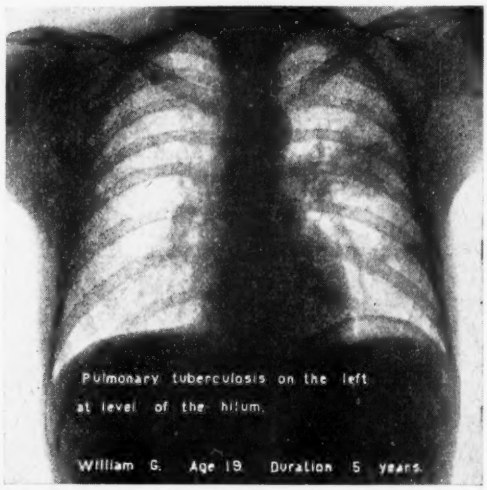

FIG. 3. Case No. 5932, January, 1932. Coma and a large carbuncle three months before discovery of tuberculosis. See fig. 4.

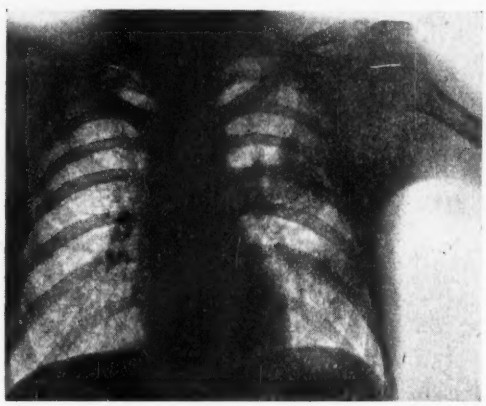

FIG. 4. Case No. 5932. Same patient as fig. 3 two months later showing extension to a wedge-shaped area at right apex and increase in process on the left. In October, 1933, he had gained 30 lbs. and was discharged from the Sanatorium. X-ray is reported "High diaphragm on the left. Fibrosis in left upper third. Healed lesions."

chronicity of pulmonary tuberculosis overshadows any one type.

Cavitation. The most conspicuous feature of diabetic roentgenogram is the large number of cavities. Forty-one or 46 per cent of the 89 cases have cavities varying in size from 0.5 cm. to 8 cm. in diameter. Multiple cavities occurred in 11 cases. In 24 cases the total diameter of cavities was 3 cm. or more. An attempt to differentiate soft-walled cavities and those with fibrous walls is bound to be somewhat unsatisfactory. However, in 28 the walls appeared definitely fibrous, indicating a less acute process than in those with soft walls.

The upper lobes were almost universally the site of cavitation. Case No. 4232, aged 18 years, had a cavity in the right lower lobe which eventually healed. In seven cases with multiple cavities, the middle on the right or the left lower lobe contained a cavity. Twenty-four cavities occurred in the left and 23 on the right.

Exudative vs. Productive Reactions. Allergy. Wassmund[31] reports that of his 60 cases of diabetes and tuberculosis, 25 were exudative, 23 were productive and 12 were mixed in type. Rosenberg and Wolff[21] considered that 27 of these 40 cases were chiefly exudative in type.

The distinction is a difficult one to make, especially in a living patient. The exudative, or inflammatory reaction, produced by fresh contact of masses of bacilli with tissues rendered hypersensitive by the primary infection may be massive and fairly rapidly involve a whole lobe, resembling lobar pneumonia in its distribution. Or it may be patchy, deep in the lungs of the bronchopneumonic type. Such infiltrations may lead to rapid destruction and cavitation, or may resolve like an ordinary pneumonia. Rapidly caseating processes, also leading to softening and cavitation, are generally considered to be conditioned by the hypersensitive state of the tissues. The involvement of serous membranes is a typically exudative reaction. In contrast are the lesions characterized by proliferation of cells, and fibrosis, leading to scarring.

We have analyzed the films of this series making use of the terms "infiltration" to include haze, mottling and consolidation as they are ordinarily used by roentgenographers. I am indebted to Dr. I. K. Bogan for the interpretations. In this series the outstanding feature is the conglomerate character of the findings. In very few films are the changes purely of one type or another. In four, Case Nos. 8435, 4763, 2448 and 5932, the exudative character of the lesions was outspoken. (See figure 5.) Mixed types constitute the great majority.

Healing—The evidence of healing in diabetic pulmonary tuberculosis is greater than expected. Autopsy reports are given in Chap. I, *New Eng. J. Med.*, 210 [Jan. 4] 1934. A considerable number of diabetics with tuberculosis in youth or middle life survive many years of diabetes without breaking down. Case No. 10036 had fever and hemoptysis at 20 years, with definite exposure to an open case, and upon advice moved to Colorado. He recovered and developed diabetes at the age of 65 years. Now at the age of 70 he weighs 180 pounds, takes 30 units insulin a day and is in good health. The apices are dull to percussion.

Healing of a cavity has occurred in at least two cases, Case No. 4232, whose roentgenograms appear in figures 6, 7 and 8, and Case No. 5231, who died later of coronary thrombosis. Case No. 3775, dentist, aged 62 years, gained 30 pounds under treatment with insulin and a cavity decreased in size.

Roentgenograms give valuable support for the belief that pulmonary tuberculosis in the dia-

betic would heal fully as well as in the non-diabetic provided that the diagnoses were made earlier, and treatment for the two conditions was adequately administered. Healed lesions

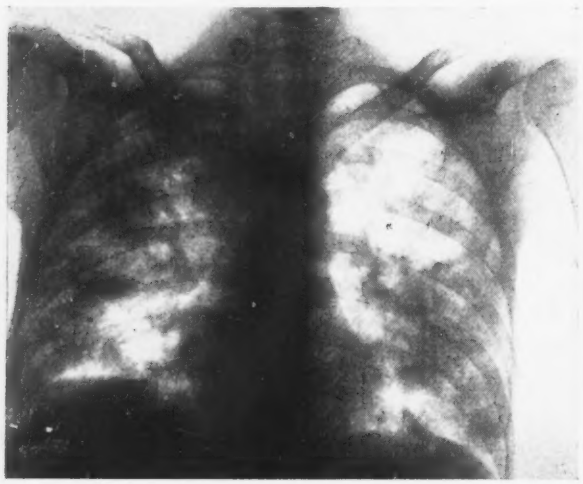

FIG. 5. Case 2448, M Aged 24 yrs., January, 1928. Duration of diabetes 6.2 yrs. Died of tuberculosis February 20, 1928.

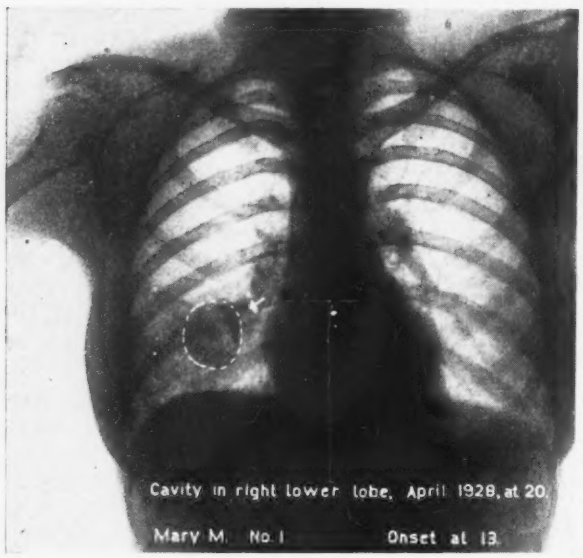

FIG. 6. Case 4232, F. Aged 13 yrs. at onset of diabetes. Cavity in right lower lobe at 20 years after repeated attacks of coma.

are dense and sharply delineated from the normal tissue; they are usually accompanied by calcified lymph nodes at the hilum and often the interlobar pleura is visibly thickened. The almost constant appearance of multiple areas of calcification in the parenchyma of diabetic lungs indicates that smaller foci of infection have been healed. Many of the rapidly fatal cases reported in the literature represent terminal states in patients whose tuberculosis really began years before.

4) Diagnosis.

a) Intracutaneous tuberculin tests. The Mantoux technique has been used almost exclusively with doses of 1 mg. and occasionally 2 mg. In 97 diabetic children positive reactions, indi-

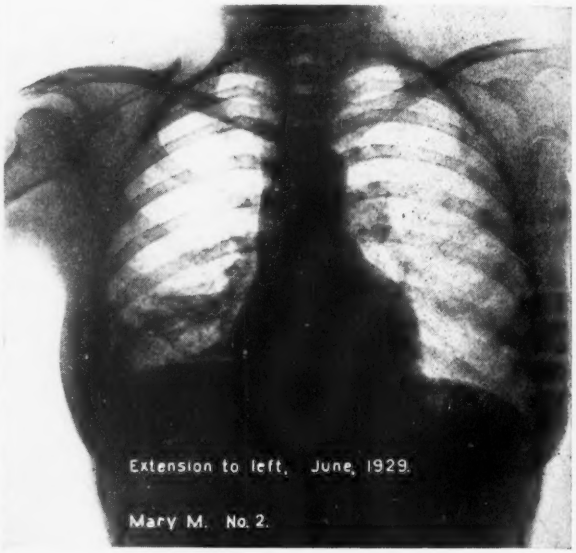

FIG. 7. Case 4232, F. Aged 21 yrs. Extension into left lung.

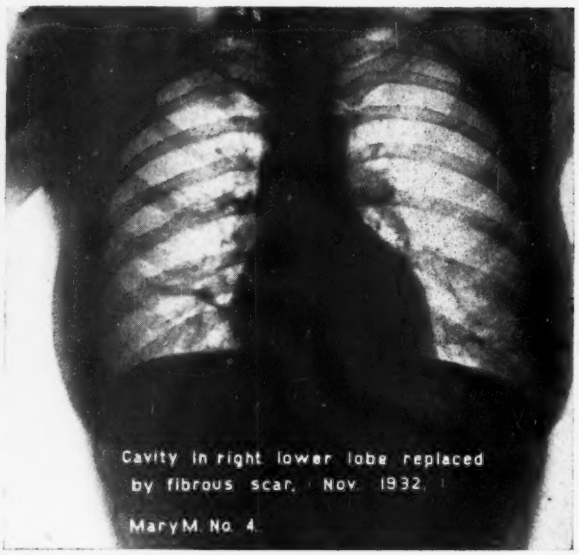

FIG. 8. Case 4232, F. Aged 24 yrs. Quiescence of tuberculosis in left lung and cavity replaced by scar. Living at home August, 1933.

cated by a zone of inflammation, often with hyperemia of 0.5 cm. in diameter have been obtained in 47. Labbé[50] has suggested that one reason for the development of tuberculosis in diabetics is the disappearance of the allergic and resistant state during acidosis. Labbé and Boulin[37] reported only one negative tuberculin test in 15 performed upon diabetic patients in 1924.

The quantitative intradermal test recommended recently by King[38] for distinguishing active from latent or healed tuberculosis in the adult

has not been used. He found that an area of erythema, usually indurated, 1 cm. or more in diameter, following the intradermal injection of 0.1 cc. of 1:20,000 dilution of human tuberculin was a reliable indication of the presence of active tuberculosis in 90 per cent of 225 cases. Schwartz and Heise using old tuberculin prepared at the Saranac Laboratory were unable to obtain with repeated tests evidences of changing sensitiveness parallel with changes in the pulmonary lesion. No such quantitative study has been made among diabetics. The most intense reaction I have observed, occurred in Case No. 4296. The intradermal injection of 0.1 cc. of 1:1000 tuberculin produced an indurated area of erythema 4 cm. in diameter with eventually a small slough. This patient had calcified tracheobronchial glands and ascites presumably due to tuberculous peritonitis. The specific character of the response to tuberculin has been brought into question. Apparently old tuberculin and the new MA 100 human proteins when given in small doses provoke a response which may be regarded as specific for tuberculous infection, according to the work of Mariette and Fenger[39]. The new preparation MA 100 obtained from different types of tubercle bacilli and timothy grass bacilli can be prepared in a purified form and can be measured more accurately than old tuberculin. It is therefore recommended as more suitable for testing purposes. Diabetic patients have not in our experience shown any greater tendency to serious reactions following intradermal tests than non-diabetics.

b) *Physical Signs.* No evidence exists that tuberculosis in a diabetic exhibits different physical signs from those found in a non-diabetic. Two diabetic conditions, however, tend to make easy the failure to discover the physical signs, great emaciation and severe acidosis. When emaciation and weakness are extreme respiratory movements are feeble, cough is absent and the clinical chart may show no abnormality of temperature, pulse or respiration. The thinness of the chest wall may yield a deceptive resonance in spite of pulmonary infiltration. Râles are so distant and fine due to the feebleness of respiration that they are scarcely audible. In such patients tuberculosis is easily missed.

In coma the respirations are deep and rapid. A peculiar amphoric quality is audible all over the chest. An over-expansion of the lungs results in deep excursion of the lung bases. Râles and changes in character of the breath sounds over an area of moderate size are frequently completely drowned out or overshadowed by the loud breath sounds from the remainder of the lung.

Differential diagnosis in early cases must include hyperthyroidism and acute pulmonary infection. In six cases with pulmonary abscess the absence of tubercle bacilli and occasionally the rapid improvement of the abscess have settled the question. Neoplasms of the lung have occurred in three diabetics, in one the diagnosis was made only at autopsy, in the second physical signs due to occlusion of a bronchus led to the diagnosis, and in the third chronic cough, severe hemoptysis and physical signs of consolidation of the right upper lobe accompanied a roentgenogram showing a dense homogenous shadow in the corresponding region. The signs produced by neoplasm vary with the size and position of the growth. There may be signs of a small area of infiltration or if the growth is larger, signs of consolidation. If the growth is larger and produces collapse of one lung from obstruction of a bronchus, displacement of the heart and mediastinum toward the affected side will be present. Variation in signs from day to day may occur due to variations in the completeness of the obstruction to the bronchus.

5) Clinical Forms. (See also Chap. II, *New Eng. J. Med.*, 210, Jan. 11, 1934.)

Pleurisy with effusion is not frequently observed. Case No. 3686, aged 66 years, died 2.5 years later of tuberculosis after the removal of 1000 cc. of clear straw-colored fluid from the right pleural cavity. Case No. 4045, a surgeon, had pleurisy with effusion at 60 years of age and 6 months later died of miliary tuberculosis.

Spontaneous pneumothorax has only been observed in four cases. Case No. 3067, housewife, entered in early diabetic coma. With 100 units of insulin she improved. Following a relapse, dyspnea and pain over the lung led to an x-ray which revealed pneumothorax and collapse of the right lung. In November, 1932, she was alive and at home although she had at one time had sanatorium treatment.

Glandular tuberculosis occurs infrequently in diabetes. Most important is the abdominal form, since attacks of pain so produced frequently must be differentiated from appendicitis, pancreatitis and diabetic coma. Case No. 4763 at the age of 16 years entered the hospital for operation with pain in the appendiceal region. X-ray showed large calcified glands in the right lower quadrant. The presence of fever and leucocytosis with some localized tenderness were confusing. However, the duration of pain was four days, she steadily improved during 12 hours' observation and operation was not performed. During the last eight years she has had no more attacks although pulmonary tuberculosis has since developed. Cases No. 10268 and 3271 presented fever, recurring attacks of pain in the right lower quadrant with leucocytosis and were operated upon. In both instances the appendix appeared normal but large mesenteric glands were observed which were regarded as tuberculous. Acute tuberculous cervical adenitis has occurred in but three cases. However, calcified cervical glands are not rare.

Miliary tuberculosis occurred in Case No.

4045, surgeon, aged 60 years and in Case No. 2687, aged 30 years.

Pneumonic types are not rare. Case No. 11471, aged 48 years had fever of 102°, rapid respiration, but little cough, signs of extensive consolidation and cavitation. At autopsy a cavity in the right upper lobe was found to have ulcerated into the bronchus, thus permitting wide dissemination of organisms. A most extensive gelatinous pneumonia was present.

One may distinguish such acutely developing pneumonia from cases with little fever or general toxic symptoms who still show by x-ray bronchopneumonic areas of infiltration. Among Sosman's 45 cases were 21 classified as of this bronchopneumonia type with the lesions at or below the level of the hilum. The prognosis was bad in all. It is not clear how many of his 21 were of the extremely acute type with death in a few weeks. In our 245 cases acute, rapidly fatal pneumonia has been rare, except as a terminal event in a chronic process as illustrated by Case No. 11471.

Atelectasis. In Case Nos. 2272 and 10163 atelectasis has occurred with retraction of mediastinum and heart. Both cases have had an extraordinarily favorable course.

6) Childhood and Adolescence. Among 201 diabetic children studied at the Deaconess Hospital 42 per cent in the first decade and 74 per cent in the second had calcified tracheobronchial glands. Forty-seven out of 97 cases had a positive Mantoux test. (See table 8.) We have very little data as to the time or the source of the primary infection. In many instances we know that a parent or relative has tuberculosis. Occasionally we obtain such a history as the following. Case No. 9535 at the age of four years had "pneumonia". For at least a month after her apparent recovery, although she seemed fairly well, she had a little fever in the afternoon. At the age of 12 years she developed diabetes and a year later was found to have calcified tracheobronchial glands and suspicious parenchymal markings. There remains a large group with positive skin tests or calcified glands without any history.

In Vienna Priesel and Wagner[40] found among their diabetic children fewer positive skin tests than among the general population. Only 68 per cent from 14 to 20 years were positive whereas in Vienna according to Hamburger and Monti (quoted by Priesel and Wagner) 94 per cent of non-diabetic 14 year old children are infected. They have observed fresh primary infection in five diabetic children from 5 to 14 years of age. In four cases the tuberculin test previously negative, became positive. The onset was pleuritic in two, grippe-like in two and in the fifth case, a large tuberculous gland developed above Poupart's ligament. The latter developed serious acidosis and for a time was refractory to insulin. In puberty they observed one case in a boy whose diabetes began at 15 years when he was tuberculin negative. He was not seen or tested until the age of 20 in February, 1930, when he had grippe, then cough and fever, night sweats and weakness. Four weeks later they found a caseous cavernous process involving the whole left upper lobe. Sputum positive. Pneumothorax did not halt the process. January, 1931, hemorrhages occurred and the right side was involved.

The Pirquet reaction was often vesicular and showed poor tendency to healing when the children had a high fasting blood sugar level. In one 12 year old child the Pirquet test was negative, but 48 hours later intracutaneous injection of 1 mg. old tuberculin led to an intense local reaction with lymphangitis, lymphadenitis and consecutive general reaction with daily fever. Therefore care should be taken with tuberculin tests with diabetic children because of the bad effect of fever upon diabetes.

TABLE 8

Incidence of Tuberculin Reactions Among Diabetic Children in Vienna and Boston

Author			*Priesel and Wagner*		
Age Years	Total Cases	Number Tuberculin Positive	Age Years	Total Cases	Number Tuberculin Positive
1-5	16	5	1-5	10	0
6-10	36	15	6-10	28	7
11-15	38	23	11-15	37	22
16-20	7	4	16-20	22	17
TOTAL	97	47	TOTAL	97	46

In their series of 97 Viennese diabetic children therefore tuberculous infection in the primary stage appears about as frequently as in our children, although our group includes more younger children. For follow-up purposes we have a much larger group (750) with onset of diabetes before the fifteenth birthday observed over a longer period of time. The development of pulmonary tuberculosis in 11 cases represents an incidence at least ten times as great as in the Massachusetts school children.

Development of Tuberculosis of adult type in Juvenile Diabetes. In table 9 are listed 17 cases

with onset of diabetes under 20 years of age who developed pulmonary tuberculosis. Eleven of the 17 were childhood cases, that is, the onset of diabetes was before the fifteenth birthday. Sexes are nearly evenly divided, in marked contrast to the cases developing later in life in which males formed 75 per cent of the group. The explanation would seem to be that the special influence upon the development of tuberculosis exerted by the more active, less sheltered life of the male is not effective till later.

TABLE 9

SEVENTEEN CASES PULMONARY TUBERCULOSIS IN JUVENILE DIABETICS

Case	Sex	Onset Diabetes Date	Onset Diabetes Age	Onset Tbc.	Diet Carb	Diet Prot	Diet Fat	Diet Cals	Cals	Insulin Units	Liv'g or Dead	Follow-up Date	Follow-up Height Inches	Follow-up Weight Pounds	Cause of Death
1555	F	1917	18	1917	90	76	75	1239	25.5	45	D	1927			Tbc.
2179	M	1921	16	1929	200					86	L	1933			
2274	M	1921	6	1927	140	81	102	1802	42.6	54	L	1933	63	93	
2448	M	1921	18	1923	100	60	100	1540		50	D	1928			Tbc. Coma
3143	M	1923	16	1925	58	54	111	1447	28.3	45	D	1925		112	Tbc.
3795	F	1923	14	1930	76	54	103	1647	39.4	5	D	1930			Tbc.
4232	F	1921	14	1928	140	72	77	1541	26.3	63	L	1933	64	129	
4743	F	1923	15	1930	177	78	126	2154	45.	30	L	1933		106	
4763	F	1925	16	1931	192	84	104	2040	35.3	62	L	1933	65	139	
5413	M	1926	15	1931	88	75	128	1804	37.6	55	L	1933		140	
5514	M	1926	6	1928	100	73	108	1664	52.9	24	L	1933	56	69	
5932	M	1927	14	1931	155	81	90	1745	34.9	60	L	1933	65	110	
6287	F	1922	7	1932	154	74	85	1677	49.3	50	L	1933	56	76	
6627	M	1927	19	1928	124	88	116	2252	42.7	52	D	1930			Tbc.
7041	M	1922	6	1929	174	55	87	1699	80.9	16	D	1930		41	Tbc.
10657	F	1928	15	1931	101	71	84	1444	32.8	54	L	1932	60		
3957	M	1924	12	1932						35	L	1933	67	140	
	10M 7F														

Every case received insulin at some time. The durations of life after discovery of tuberculosis in six fatal cases were 9.8, 4.5, 0.7, 0.9, 2.0 and 0.2 years respectively, and all died of tuberculosis. In 11 cases still living the average duration of the diabetes is 9.0 years and of the tuberculosis is 3.0 years. Family exposure was known in eight cases, but we have no satisfactory data regarding the family histories of the remaining nine cases.

CASE No. 1555. Polyuria, cough and hemoptysis began in the same month, November, 1917. February 13, 1918, the urine contained 2.4 per cent sugar, weight 107 pounds. Sputum contained many tubercle bacilli. Fever continued for six months. Insulin was begun in 1923. She married in 1924. Treatment for tuberculosis was continued at Sharon, Mass. and Lake Saranac, New York.

CASE No. 2179. One sister has diabetes. Tuberculosis developed after eight years of diabetes. In 1930 Dr. W. Bertnard Smith stated that he had involvement of both lungs with a cavity in the left, a positive sputum, but was improving. At that time his weight was 154 pounds, insulin 86 units and diet contained 200 grams carbohydrate. In December, 1932, Dr. Smith describes remarkable improvement. Fever is gone, pulmonary lesions are almost healed and he is able to do a little light work. The diet still contains 200 grams carbohydrate, 2500 calories and insulin dose is 62 units.

CASE No. 2274. His grandfather, with whom he lived, died of pulmonary tuberculosis when he was five years old. Diabetes began at six years and pulmonary tuberculosis was recognized at the age of 12 years. Sputum contained tubercle bacilli. Between the ages of 13 and 16 years he grew seven inches in height and gained 17 pounds in weight.

In the spring of 1931 he was living out-of-doors and had little cough and no sputum could be obtained during a two weeks' stay at the Deaconess Hospital in July, 1931, although he had an irregular fever. Roentgenogram of the lungs is shown in figure 9. Entered a sanatorium in 1933.

CASE No. 3795 after a short period of hospital treatment refused to answer letters or to coöperate in any way. A letter from her physician describes her terminal illness and death with advanced pulmonary tuberculosis seven years after discharge from the hospital.

CASE No. 6287 had absolutely uncontrolled diabetes from the onset of the disease in 1922 until the discovery of her tuberculosis. She had had several admissions to the Children's Hospital and 23 admissions to the New England Deaconess Hospital frequently with acidosis and coma. Her diabetes was still mild and easily controlled during her hospital stay. As a result of this uncontrolled diabetes she has failed to grow in height and had shown x-ray evidence of calcification in the vessels of the legs. Because she lived nearby, her chest was studied by x-ray every three to six months for a period of three years. The calcification in the tracheobronchial glands was observed and finally in June, 1932 an area of infiltration just below the right clavicle one inch in diameter homogeneous in density was discovered. (See figure 1.) After three months' sanatorium treatment the shadow showed fibrosis and diminution in size. She left the sanatorium against advice. In May, 1933, following eight months' neglect, tuberculosis has flared up with slight extension of the process, cough and fever.

SUMMARY

1) Diabetic children have had a primary tuberculous infection in from 42 to 74 per cent of the cases.

2) Calcified tracheobronchial glands indicate that a relatively massive primary infection was received often from an intimate contact, as in the family.

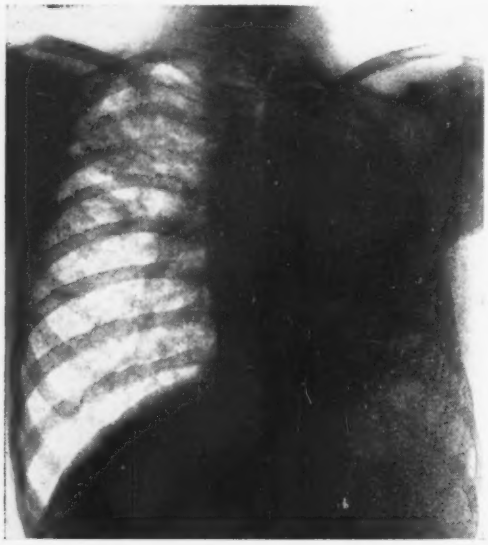

FIG. 9. Case 2274, M., aged 16 yrs. July, 1931. Duration of diabetes 10 years. From 1928 to 1931 he gained seven inches in height and 17 pounds in weight. Living July, 1933, with active pulmonary tuberculosis for at least six years.

3) Active pulmonary tuberculosis of the adult type developed in patients with onset of diabetes before 15 years at a rate at least ten times as frequently as among the school children of Massachusetts.

4) The cases of tuberculosis develop most frequently among cases with the least well-controlled diabetes, as exemplified by Case Nos. 2448, 4232, and 3795. A free diet even with insulin encourages the development of tuberculosis.

5) The pneumonic types of tuberculosis seen represent terminal stages in a slowly progressing tuberculosis. In at least two cases of this series primary foci were in the cervical gland.

6) With careful treatment of diabetes and tuberculosis, the young diabetic may have a far more hopeful outlook for healing and arrest of the tuberculosis than has appeared in the past.

Old Age and Tuberculosis Long Latent. Pulmonary tuberculosis is not limited to youth. Among the 245 cases of this series 49 were discovered in patients over 60 years of age and of these, 14 were over 70 years of age. Rubin[48] analyzed records of 414 patients with pulmonary tuberculosis over 50 years of age treated at the Montefiore Hospital, New York. Among these were 72 or 17 per cent with diabetes.

Certain cases represent chronic tuberculosis with slow progression in whom no special influence on the part of diabetes can be traced. Case No. 3141, real estate dealer, developed diabetes in 1918 at the age of 48 years. In 1909 his doctor had diagnosed pulmonary tuberculosis because of cough, hemoptysis and apical râles. He began insulin in May, 1924, with five units. In January, 1932, his weight was 147½ pounds, his insulin 12 units. He denied cough, but on "clearing his throat" purulent sputum, with many tubercle bacilli, was obtained. X-ray examination—"The hila are large with small calcium deposits. Running outward from the left hilum there is marked peribronchial fibrosis in the second interspace and two cavities, one directly beneath the other. The larger, upper one is two and a half cm., the lower, one and a half. The upper interspaces on the right are very narrow, and the chest decreased in width. The apex and first interspace are dull, and below this there is diminished density. The trachea is displaced to the right. There is an area of dulness in the third interspace approximately two and a half cm. in length. Chronic Tuberculosis."

The onset of diabetes late in life may cause a relighting of an old smouldering infection. Case No. 5976 developed diabetes at the age of 63 years. X-ray examination of her lungs in 1929 showed only calcified tracheobronchial glands with a few fibrous strands at the apices. She developed angina pectoris and a large liver, possibly due to cardiac incompetency. She returned to the Deaconess Hospital later with cough, a positive sputum and x-ray findings as shown in figure 10.

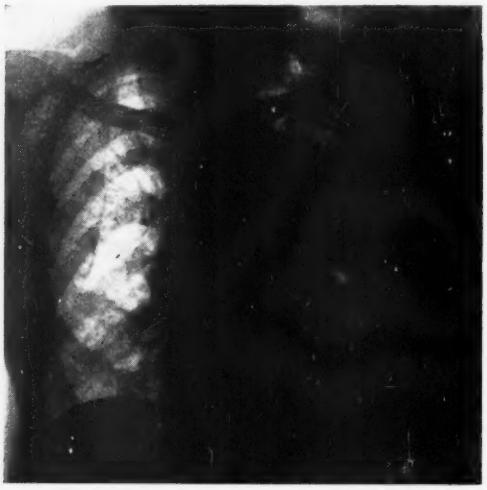

FIG. 10. Case 5976, F., 72 yrs. Duration of diabetes 9.8 yrs. in October, 1930. Sputum positive. X-ray negative in 1929 except for calcified glands and fibrous strands toward apices. Died of tuberculosis December, 1931.

Case No. 398 had pleurisy with effusion at 17 years. His father died of phthisis when he was 10 years old. His mother had diabetes. He was sickly till his early twenties. During the years until he was 65 he lived an active life as head of a business, and prominent in community affairs. He developed diabetes at 44 years, angina pectoris at 66 and pulmonary tuberculosis with positive sputum at 69 years. Death in May, 1933, at the age of 73.

Case No. 1977 developed diabetes at 71 years.

At the age of 79 years she entered the Palmer Memorial for permanent care. She had no cough, no fever during two years of her stay. A week before her death at the age of 81 years she developed fever and cough with signs interpreted as due to bronchopneumonia. At autopsy chronic pulmonary tuberculosis of the left upper lobe was found. (See Chap. I, *New Eng. J. Med.*, 210, Jan. 4, 1934.)

Such cases are not rare and may lead us quickly to conclude that the onset of diabetes late in life induces such a breakdown when no opportunity for exogenous re-infection is known. However, it is easy to match such cases by many others with known tuberculosis in youth who have survived many years of diabetes without an activation of pulmonary tuberculosis. Case No. 1257 (see Chap. I, *New Eng. J. Med.*, 210, Jan. 4, 1934 for autopsy) died after 25 years of diabetes, yet her apical lesions remained perfectly healed.

8) Rate of Progression: The unfavorable prognosis so generally given to diabetic tuberculosis does not take into account the long period of unrecognized tuberculosis. No satisfactory picture of the progress of a pulmonary lesion in a diabetic can be secured from physical signs, symptoms, temperature and pulse charts, weight record or blood sugar. Definite and rapid progression can occur without any reflection in these criteria. Infiltration and excavation can progress for months without the development of noticeable signs or symptoms. Only when adequate chest films are taken at regular intervals can we appreciate the changes taking place. In Case No. 4045 in an interval of six weeks without symptoms miliary tuberculosis developed with fatal termination six weeks later. Yet cases recognized in an early stage, such as Case No. 7263 with a minimal lesion below the right clavicle may remain stationary for many months.

Ornstein et al[41] have described an acute form of tuberculosis occurring in a series of 58 non-diabetic cases. Onset was sudden, symptoms slight (cough, expectoration, often hemoptysis) and soon disappeared. Within a few weeks or months the dense pulmonary shadows disappeared. Such cases are not as yet reported among diabetics, yet Case No. 4232, proves the remarkable arrest of extensive processes that may occur even in diabetics. Fitz also describes a man, aged fifty-two years, who came to the Outdoor Department in October, 1927, weighing 160 pounds and with diabetic symptoms of about a year's duration. A roentgen ray of the chest revealed no abnormality. His diet did not keep him sugar-free but he lost 20 pounds in weight during the following three months. During this interval he developed cough, chest signs, positive sputum and a lesion at the right apex. As measured by roentgen ray the process extended as low as the level of the fourth rib.

When the tuberculosis was recognized the man was put in bed at absolute rest for a period of six weeks. He was given a liberal diet and enough insulin to prevent glycosuria. Now, more than two years later, he has no signs of tuberculosis. Physical and radiologic examinations are negative and the diabetes is controlled.

The general condition of the patient, the duration and extent of the lesion, and control of the diabetes are factors in determining the rate of progression or healing.

9) Complications. Degenerative changes characteristic of uncontrolled diabetes occurred in this group. Cataracts developed in Case No. 5932 at 17 years and Case No. 4232 at 20 years. Both these patients had coma and carbuncles and calcified arteries in the legs. Coronary disease with angina pectoris occurred in Case Nos. 398 and 177.

Cirrhosis of the liver occurred in Case No. 6725 with ascites and edema. Cordier and Sédallian[42] described a woman 48 years of age with alcoholic cirrhosis of the liver, jaundice, diabetes and tuberculosis, who died of intestinal hemorrhage. They report three other cases of combined diabetes and tuberculosis.

Syphilis was present in Case No. 8967 with general paresis. She received vigorous antiluetic treatment in 1929 and is still living. Case No. 7143, female, aged 41 at onset of diabetes and 45 years at onset of tuberculosis did not receive intravenous antiluetic treatment because of the advanced stage of the tuberculosis. Case Nos. 2518 and 6184, male, developed diabetes at 47 and 23 years, tuberculosis at 51 and 52 and died at 51 and 55 years without antiluetic treatment.

Laignel-Lavastine[43] et al describe a 15 year old boy, son of a luetic father, whose tuberculosis progressed in spite of insulin and pneumothorax. Charcot knees, tabes dorsalis, syphilitic aortitis, a large tuberculous cavity in the right upper lobe and diabetes were combined in a man 50 years of age reported by Ellman[44]. Intensive arsphenamine treatment was given a diabetic girl, 16 years old with pulmonary tuberculosis and Landis[45] reported disappearance of pulmonary symptoms.

Pregnancy terminated normally in Case 3040. She developed diabetes at 10 years, was married at 17 years. X-ray examination showed large calcified glands at the hilus with a calcified primary focus in the outer parenchyma. In spite of three attacks of coma, frequently broken dietary rules, no pulmonary process has so far broken out. However, she does have an indolent, possibly tuberculous ulcer of one leg. On June 1, 1933, she weighed 147 pounds, diet carbohydrate 177 grams, protein 84 grams, fat 90 grams, insulin 56 units.

Silicosis was recognized in Case No. 10548, quarry man, aged 65 years. He also had pri-

mary hyperthyroidism, advanced arteriosclerosis, left bundle branch block as indicated by electrocardiogram, and underwent a successful operation upon the thyroid. Epileptiform convulsions occurred in two cases; the first described by Chauffard and Rendu[46], a man, 49 years old, alcoholic, with pulmonary tuberculosis died after a series of 35 convulsions. Blood sugar was 0.20 per cent. Autopsy showed no renal or cerebral disease except abundant cerebrospinal fluid. The liver was scirrhotic. Arteriosclerosis was present although diabetes was of only four years' duration. Achard's[47] case was a girl, 25 years old with diabetes for six years and active pulmonary tuberculosis. She developed right hemiplegia and Jacksonian epilepsy.

Surgical operations have been performed without ill effect upon tuberculous diabetics. Case No. 5932 had an acute appendix removed at the Rutland Sanatorium.

Gangrene. Sixteen cases of gangrene occurred among the 245 patients. The youngest patient to develop gangrene was Case No. 6809. Diabetes began at the age of 28 and pulmonary tuberculosis at the age of 30 years. He entered the hospital with gangrene of one foot, with acute ascending infection of that foot, edema of the ankles and advanced pulmonary tuberculosis. A year later his brother, also a tuberculous diabetic developed gangrene at the age of 31 years. The autopsy is summarized in table I. (Chap. II, *New Eng. J. Med.* 210 [Jan. 11] 1934.)

Summary

1) Among 245 tuberculous diabetics, only 10 were discovered with a minimal pulmonary lesion. Tardy diagnosis characterizes diabetic tuberculosis.

2) Onset of tuberculosis was subsequent to onset of diabetes in 85 per cent of the cases.

3) Although both sexes were equally infected early in life, male diabetics are almost twice as likely to break down in adult life with pulmonary tuberculosis as are females.

4) The average loss of weight for 219 cases was 42 pounds and in 24 cases the average was 88 pounds.

5) Marked gain in carbohydrate tolerance during advancing tuberculosis occurred in a few cases.

6) Blood and urine chemistry and data of the respiratory metabolism preceding the development of tuberculosis in 8 cases are summarized.

7) Comparison of onset, symptoms and physical signs with those in non-diabetics shows no special insidiousness in the development of tuberculosis in the diabetic.

8) Roentgenograms of the lung in 1659 consecutive diabetics and of 87 cases with proved tuberculosis are analyzed. Multiple areas of calcification indicating former infection are the rule. Moderate and advanced processes formed 89 per cent of the tuberculous cases. No special diabetic type of lesions was observed, although exudative, pneumonic types with cavitation frequently developed in patients with evidences of previous infection.

9) The incidence of pulmonary tuberculosis increases with the duration of the diabetes. Among 19 males with diabetes over 20 years 3, or 16 per cent had active pulmonary tuberculosis.

10) In childhood skin tests with tuberculin were positive in 46 per cent of cases both in Boston and in Vienna. Among 201 diabetic children calcified tracheobronchial glands were found in 42 per cent in the first decade and 74 per cent in the second decade of life.

11) Seventeen cases of adult type tuberculosis in juvenile diabetics are summarized. Eleven are still living with diabetes of nine years' duration and tuberculosis of at least three years' duration.

12) In 49 cases tuberculosis developed after the age of 60 years. Processes apparently latent for years developed activity after onset of diabetes.

13) Complicating pregnancy, gangrene, syphilis and cataracts are recorded.

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ARTHRITIS AND SYSTEMIC INVOLVEMENT AS EXEMPLIFIED IN A GROUP OF DEAD ARTHRITICS*

BY H. ARCHIBALD NISSEN, M.D.,‡ AND K. A. SPENCER‡

OUT of a group of 341 arthritic patients studied in the Survey of Chronic Disease at the Robert B. Brigham Hospital, 95 died during the years from 1914 to August, 1933. The life histories of these dead have been reconstructed on a basis of yearly divisions, thus clarifying the functional activity at a given period; the remissions and relapses of arthritis, and the relationship between arthritis and systemic involvement, and disease entities. The primary object of this study was to determine if there were relationships between joint and skeletal changes and involvement of the other body systems. The actual joint involvement was not stressed. Previous papers† noted the involvement of several body systems in the majority of arthritics, antedating, coinciding with, or following the onset of arthritis. The question of cause or effect, whether arthritis is the cause of or the result of these systemic involvements, remained unanswered. It seemed obvious that in the dead, whose cycle of life was completed, the dovetailing of systemic dysfunction could be best demonstrated. In such a review, hindsight enables one to interpret accurately as definite onset of disease, former vague symptoms which were impossible to evaluate at the time of complaint. Twenty-one of the 95 dead were examined postmortem.

Many of the group were followed to death by members of the Robert Brigham Hospital Staff. Others were lost during the years, and died at home or in other institutions. It is due to the helpful coöperation of other hospitals, social agencies and relatives that the life history of practically the entire group was completed, and the Robert B. Brigham Hospital wishes to express here its deep appreciation of this assistance.

During the analysis, another fact became evident. This was that the 95 dead followed four distinct, definite paths to the grave, irrespective of the type of arthritis, the age at onset, or the age at death; the duration of the disease; single or multiple systemic involvement; environment, family tissue inheritance; occupational hazard; carrying little or great extra load of infection; worry or emotional strain. In other words, individual reaction apparently determined the life course rather than any one, or all, of the above factors. There is much to indicate that joint change is but a small portion of a problem which in the arthritic embraces a psycho-physio-chemical reaction. Possibly the same thing is true in all chronic disease. These Life Courses have been termed for convenience, A, B, C, and D. It must be emphasized that they indicate the patient's *life* course (not merely his joint course), his functional activity from year to year. Functional activity was influenced chiefly by the degree of joint involvement, but it was also affected by disability due to other systemic disease. The life course was drawn from an arbitrary one hundred per cent, indicating that individual's optimal activity, to zero, or death. From one hundred per cent to seventy-five per cent he was ambulatory with little actual functional handicap. From seventy-five to sixty per cent he continued ambulatory but to a lesser extent and with increasing handicap. At fifty per cent he had reached the level of chair life. From fifty per cent to twenty-five per cent he was definitely confined to chair or bed; and at twenty-five per cent he had reached a state of almost complete helplessness and deformity. Representative charts demonstrate each Life Course.

Course A represents the individual who, with the onset of arthritis, drops to a lower level of

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†Sugar Tolerance in the Arthritic: Arteriosclerosis in the Arthritic. Nissen and Spencer. N. Eng. J. Med. 210: 13 and 92, 1934.

‡Nissen—Spencer—For records and addresses of authors see "This Week's Issue," page 162.

activity, the degree of the drop being variable, remains there for a period of time; then, because of better tissue inheritance, determination, successful treatment, or natural individualistic reaction, climbs back toward his former level of activity, and retains this level throughout the greater part of his remaining life.

Course B, after the initial attack of arthritis, again of varying duration, shows definite periods of remission and relapse throughout the rest of life. As the years pass, however, there is a trend for the periods of relapse to lengthen and become more frequent as those of remission shorten and occur less often. A mean line drawn through these plateaux shows a slow, steady slant downward.

In Course C, the individual goes along to a certain point at which he receives some severe systemic, cataclysmic upheaval, infection or functional disturbance, and goes down with a crash. There is rapid and devastating involvement of all joints, and in a period of months to a few years he eventually strikes bottom at a low level of activity. At this level of crippled helplessness he continues, often for years, with surprising immunity to any acute infection, and with relatively minor ups and downs until death. This long survival at a minimal level of function is made possible in many instances by the patient's ability to develop and build up a new motivation for living.

The patient following Course D averages the shortest life line. With either an acute or insidious onset of arthritis, with a rapid or slow joint involvement, the course is a steady progression downward to death. This suggests that in patients suspected of falling into this group, infected tissue, even as definite foci of infection, may better be left alone rather than attempt made to eradicate it, because the consequences attendant on anesthesia and postoperative shock are so often dire.

It is apparent that patients in Course A and Course B are those who respond most satisfactorily to treatment. Those in Course C and Course D represent the problematical group on

SUMMARY OF WORKING CHART

Life Course	Total Number	Sex		Arthritic Type						
		Male	Female	1	2	Mixed	Strumpell-Marie	G. C.	Still's	Rheum. Fever
A	5	1	4	1	1	3				
B	51	24	27	10	23	12	5			1
C	13	5	8	8		4			1	
D	26	13	13	8	6	7	3	1	1	
Total	95	43	52	27	30	26	8	1	2	1

Life Course	Average Age Onset	Average Age Death	Duration of Life After Onset of Arthritis					
			Average Years	1-10 Years	11-20 Years	21-30 Years	31-40 Years	Over 40 Years
A	27.6	54.6	27		1	2	2	
B	40.5	57.8	17.3	14	20	13	3	1
C	39.4	58.5	19	3	3	7		
D	39	46	7	21	5			
Total	38.8	54.2	17.5	38	29	22	5	1

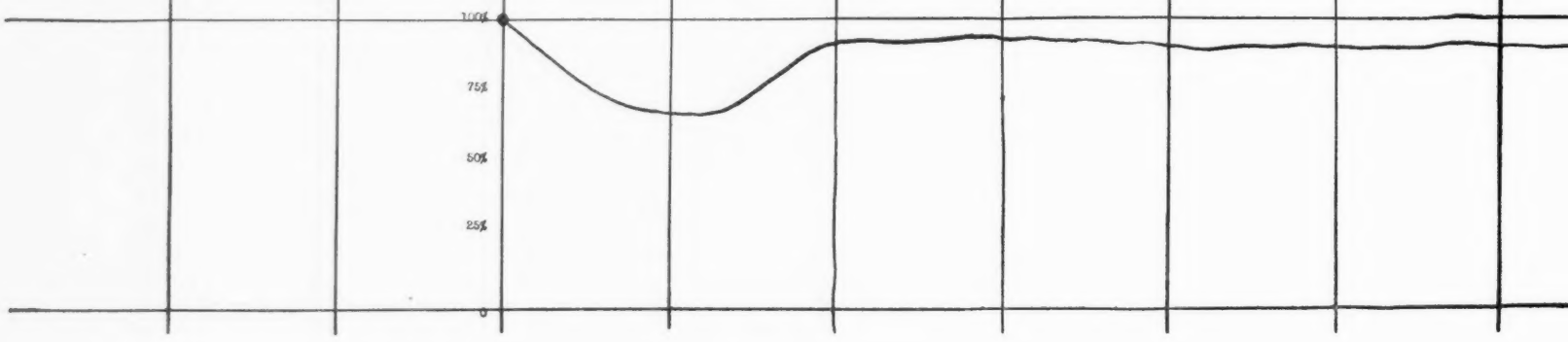
Life Course	Other Systems Chronically Involved								
	Cardio-circulatory	G. U. Tract	G. I. Tract	Blood	Tissue Change	Respiratory	Endocrinal	Eyes	Skin
A	4	3	3	1	3	3		2	1
B	39	28	24	16	27	17		9	
C	8	10	5	2	3	5		4	1
D	19	17	10	10	18	5	1	3	1
Total (95)	70	58	42	29	51	30	1	18	3

Life Course	Number of Other Systems Involved in One Case							
	None	One	Two	Three	Four	Five	Six	Seven
A			1	1	2		1	
B		7	11	18	6	6	2	1
C	1		6	3		2		1
D	1	3	4	9	4	4		1
Total (95)	2	10	22	31	12	12	3	3

FEMALE - MIXED TYPE ARTHRITIS

TYPICAL LIFE-COURSE A

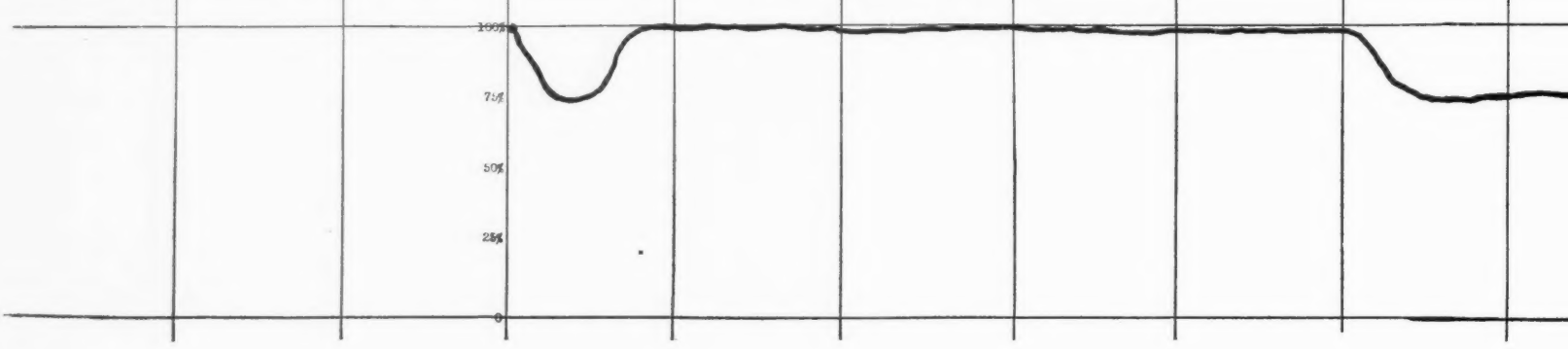
PRODROMAL	ONSET	1st year	2nd year	3rd year	4th year	5th year	6th year	7th ye
	AGE 20 years	20-21 years (1903)	21-22 years(1904)	22-23 years (1905)	23-24 years (1906)	24-25 years (1907)	25-26 years (1908)	26-27 yea
Family History: Tissue inheritance, Fair Marital History: Sufficient cause to produce emotional upset Past History: Measles, scarlet fever, bronchitis in childhood At 15, Catamenia " 20, married	Following injury in left heel from rusty nail, ankle became stiff, and painful.	Walking became difficult. Shortly afterward similar involvement right ankle	Both wrists and hands became swollen, stiff and painful. Gradual improvement By end of year, practically complete recovery except for limited motion and some deformity in left ankle and hands	NO JOINT SYMPTOMS			FOR	



FEMALE - TYPE 1 ARTHRITIS

TYPICAL LIFE-COURSE B

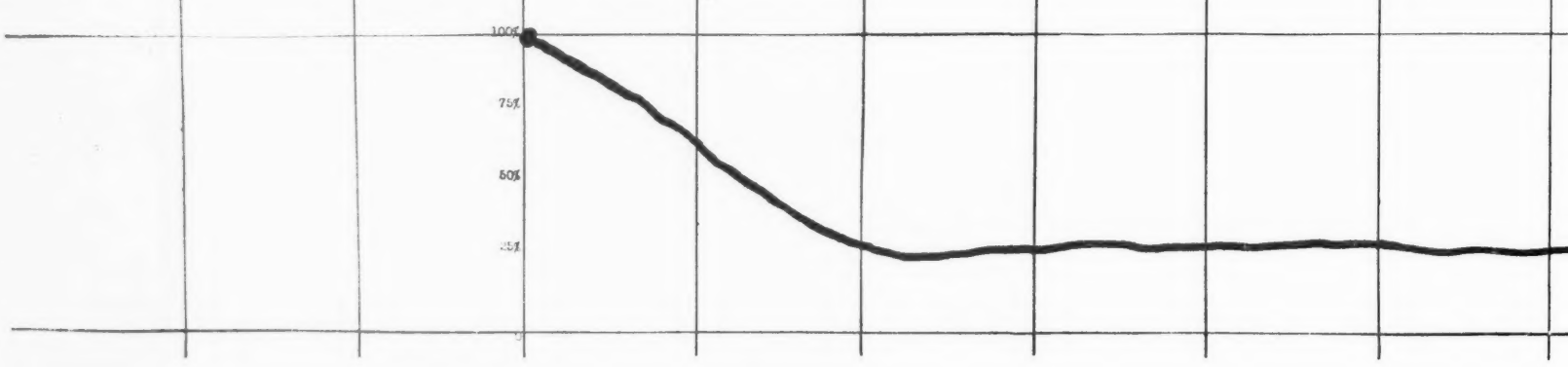
PRODROMAL	ONSET	1st year	2nd year	3rd year	4th year	5th year	6th year	7th y
	AGE: 39 years	39-40 years (1913)	40-41 years (1914)	41-42 years (1915)	42-43 years (1916)	43-44 years (1917)	44-45 years (1918)	45-46 y
Family History: Tissue inheritance fair. 1 sister died of tuberculosis Marital History: Negative, except subsequent emotional strain Past History: Usual diseases of childhood Deaf from childhood Cervical Adenitis	Onset of Pain in shoulders, elbows and hands.	Hospital 3 months; complete recovery.	Well	Well	Well	Well	Menopause Influenza with subsequent stiffness and pain in knees and ankles Treated with massage and manipulations	Condit same year



MALE - TYPE 1 ARTHRITIS

TYPICAL LIFE-COURSE C

PRODROMAL	ONSET:	1st year	2nd year	3rd year	4th year	5th year	6th year
	AGE: 48 years.	48-49 years (1905)	49-50 years (1906)	50-51 years (1907)	51-52 years (1908)	52-53 years (1909)	53-55 years (1910)
Family History: Nerve inheritance poor. Marital History: Irrelevant as given. Past History: Scarlet fever, Measles and other children's diseases in childhood At 18, attack of lead poisoning colic At 43, accident, crushing left foot	Onset of swelling in left leg, extending from knee to toes; pain, redness and tenderness.	1 month after onset, right leg similarly affected. Pain and swelling remained present. Process spread, and within two years, hips, elbows, wrists, shoulders and hands involved The hands were swollen but finger joints were not swollen or painful Diagnosed as rheumatism, caused by lead poisoning Moderate Drinker WEIGHT AT ONSET 130# -	STEADY LOSS	JOINT CONDITION OF WEIGHT	REMAINED	UNIMPROVED	



7th year	8th year	9th year	10th year	11th year	12th year	13th year	14th year	15th year	16th year	17th y
26-27 years (1909)	27-28 years (1910)	28-29 years (1911)	29-30 years(1912)	30-31 years (1913)	31-32 years (1914)	32-33 years (1915)	33-34 years (1916)	34-35 years (1917)	35-36 years (1918)	36-37 year
N E X T	Gonorrhea T W E N T Y	OPERATION: Right salpingectomy: Appendectomy: Ventral Suspension Y E A R S Leukorrhea following operation	E X C E P T	F O R T R	A N S I E N T	Positive fixation of blood for gonorrhea J O I N T P	A I N O R	T I F F N E s	S N O L I	I T A

7th year	8th year	9th year	10th year	11th year	12th year	13th year	14th year	15th year	16th year	17th y
45-46 years (1918)	46-47 years (1920)	47-48 years (1921)	48-49 years (1922)	49-50 years (1923)	50-51 years (1924)	51-52 years (1925)	52-53 years (1926)	53-54 years (1927)	54-55 years (1928)	55-56 years
Condition about the same as previous year	Fell, striking back on street curb. Ill 2 weeks. Later in year, mild right-sided pleurisy. Joint condition continued present with remissions and relapses.	Teeth extracted with subsequent temporary relief of joint symptoms	Year of remission	Year of remission	Developed slight dyspnea on exertion Involvement of both hips in arthritic process. Entered another hospital. Casts were applied to both legs for some weeks. After removal of casts, unable to walk or even dress herself. Shoulders, elbows, hands, hips knees and ankles now affected. CONTINUED TO BE	BEDRIDDEN	JANUARY: Admitted to Robert Brigham Hosp. C.C. Complete disability from arthritic involvement; slight dyspnea on exertion P.E. Poorly nourished; Wt. 100# Ht. 5' 7¼" Deaf; vasomotor instability evidenced by cold sweating hands JOINTS all show limited motion; no actual ankylosis; ulnar deviation of fingers; atrophic skin BLOOD Anemia X-RAY: G I. tract, stasis ? appendix. Bone atrophy; destruction cartilage; thinning and erosion bone; some regenerative changes; narrowing and some obliteration joint space BASAL METABOLISM always low; thyroid medication given during most of hospital stay. Steady gain throughout year. Gradually gotten up in chair; then to walking a little. Blood count rose	Continued improvement, in general health, strength and joints Chronic blepharitis appears Blood count up to nearly normal Up in chair and walking some daily	FEBRUARY: Fell, striking on back. Bed for a month; febrile reaction JUNE: Apparently back to nearly former status No active arthritis GAIN of 16# in weight since admission to hospital. (3 years)	Return of anemia,- Pernicio 3 months l count ba with tra patient d strength. X-RAYS: l arthriti Slow grad through weeks o alterna weeks o

7th year	8th year	9th year	10th year	11th year	12th year	13th year	14th year	15th year	16th year
(1910)				58-59 years (1915)	59-60 years (1916)	60-61 years (1918)	61-62 years (1918)	62-63 years (1919)	63-64 years (1920)
EDEMA OF FEET AT NIGHT - DISAPPEARING IN THE MORNING FUNCTIONAL	Onset of DEAFNESS STATUS,- B E D R I D D E N or C H A I R L I F E	DEAFNESS	INCREASING FREQUENCY and NYCTURIA appear	FEBRUARY: Admitted to Robert Brigham Hosp. P.E. Poorly developed and nourished. SKIN dry and scaly: very DEAF: TEETH out except one carious one: TONSILS present: CHEST, old rachitic deformity; LUNGS hyperresonant: BLEPHARITIS. JOINTS all involved; some ankylosis; deformity; restricted motion. Knees permanently flexed; left knee painful and swollen; active arthritic process X-RAY: Atrophy soft parts and bone; destruction cartilage and bone; also hypertrophic and infectious changes G.I. Tract: Gastro-enteroptosis; ileal stasis; fixed cecum URINE v.s.t. albumin B.P. 140/80 BED or CHAIR life. NYCTURIA and CONSTIPATION present JUNE: Otitis media; duration 20 days JULY: Localized Erysipelas SEPTEMBER: Abdominal pain; cramps; fever 101° duration several days DECEMBER: Slight improvement	JOINT condition remains about the same Intermittent attacks abdominal pain; more complaint of constipation; some dysuria from time to time. W H E E L C H A I R O R B E D U R I N E S H O W E D C O N S T A N T L Y	CHIEF COMPLAINTS: Constipation with abdominal discomfort: chronic dysuria	Several head colds SEPTEMBER: Transferred to Convalescent Home during Government occupancy of Robert Brigham Hospital. Continued under Staff supervision.	THREE OUTSTANDING COMPLAINTS: and INDIGESTION JOINTS PRACTICALLY INACTIVE irritation from time V A R Y I N G N U M B E R S W.

17th year	18th year	19th year	20th year	21st year	22nd year	23rd year	24th year	25th year	26th year	27t
36-37 years (1919)	37-38 years (1920)	38-39 years (1921)	39-40 years (1922)	40-41 years (1923)	41-42 years (1924)	42-43 years (1925)	43-44 years(1926)	44-45 years (1927)	45-46 years (1928)	46-47
				Attacks of syncope with palpitation; some dyspnea; rare precordial pain.		OPERATION: T. & A.	Upper teeth extracted, some of which were abscessed	Beginning of diminution of menstrual flow	AUGUST: Acute pain and soreness with swelling in elbows and knees, following a typical sore throat and attack of bronchitis.	FEBRU
									SEPTEMBER 1928 admitted Robert Brigham Hospital Joint flare-up subsiding at time of admission.	APRIL ethm Righ Exci
L I M I T A T I O N	O F	F U N C T I O N A L	A C T I V I T Y						P.E. TEETH:Upper plate; caries lower jaw; HEART: Systolic murmur harsh second sound JOINTS: Moderate limitation motion left elbow and wrists; thickening and slight deformity finger joints. No pain or redness of these joints. Crepitus and pain on motion of knees; limited motion ankles. Height 5'4½" Wt.125# B.P. 112/74 Blood normal X-RAY:Multiple arthritis with punched-out areas. Destruction cartilage. Erosion and atrophy of bone;narrowing joint spaces. Question right frontal sinus. Hilus density chest. Atonic stasis in G.I. tract. OCTOBER: Substance joint symptoms up part each day. NOVEMBER:Complaint substernal discomfort; sense pressure;no cough or fever. 7 foot x-ray negative Joints comfortable except left shoulder and elbow. DECEMBER: Upper respiratory tract infection.	MAY: plai ches inal pain the tion comf Disc
				F R E Q U E N T	A T T A C K S	O F B R O N	C H I T I S:	S P U T U M		LABOR sent cept capa NPN Rena Bloo
					O C C A S I	O N A L L Y B	L O O D S T	R E A K E D.		"
					N I G H T	S W E A T S :	C O N S T I	P A T E D :		Rest abou hour gree hand mild join incr
					O C C A S	O N A L P A	I N L E F T	S I D E .		of

17th year	18th year	19th year	20th year	DEATH:
55-56 years (1929)	57-58 years (1930)	57-58 years (1931)	58-59 years (1932)	AGE: 58 years
Return of marked anemia,- apparently a Pernicious Anemia	Blood count continue fairly normal.	JANUARY TO MAY able to sit in chair part of day.	JANUARY discharged to another institution.	DURATION: 19 years
3 months later, blood count back to normal with treatment but patient did not regain strength.	Continued to show gradual progressive failing.	MAY through remainder of year, bed constantly	FEBRUARY: Fluid demonstrable in right chest; continued to death	DIAGNOSES: Chronic arthritis, Type 1 Bronchopneumonia Pernicious Anemia Myocardial Failure Pleural Effusion,right (? Sepsis)
X-RAY: Increase in arthritic process	Most of day spent in chair or bed.	Increasing joint pain, shifting in location; but no acute flare up or joints or evidence of active arthritis	MARCH: Bed sores. Blood count practically normal	SUMMARY: Involved: Bone and joints Tissue (Weight loss) Blood
Slow gradual failing through year with weeks of improvement alternating with weeks of relapse.		DECEMBER: Sudden return of Pernicious Anemia, following a week of emotional strain	APRIL: Blood continues fairly normal. Increasing difficulty with bed sores. High White count	ADDITIONAL LOAD: Vasomotor Instability with emotional strain
		Increasing weakness; intermittent pain	MAY: DIED.	
100%				
75%				
50%				
25%				
0				

FEMALE - TYPE 1 ARTHRITIS

PRODROMAL	ONSET	1st year
	AGE: 41 years	41-42 years (1920)
Family History: Tissue inheritance fair	Aching pain right elbow shoulder and Ankle after use.	Attacks at first lasted a few da
Marital History: Negative except husband died of tuberculosis 1914		6 months after ons left shoulder, el and hand involved
Past History: Frequent colds At 15, catamenia " 18, pneumonia " 37, hemoptysis (2 years after husband's death) Loss of 20# that year. Spent 20 months in a Sanitarium but tuberculosis not proved " 38, pneumonia		Within the year, k and feet, in addi to other joints, stiff, swollen an painful. Joints but not red.
100% (37 years		
75%		
50%		
25%		
0		

16th year	17th year	18th year	19th year	20th year	21st year	22nd year	23rd year	24th year	25th year	2
63-64 years (1920)	64-65 years (1921)	65-66 years (1922)	66-67 years (1923)	67-68 years (1924)	68-69 years (1925)	69-70 years (1926)	70-71 years (1927)	71-72 years (1928)	72-73 years (1929)	74-75 y
COMPLAINTS: INDIGESTION	CONSTIPATION, ABDOMINAL PAIN,		Less active. More frequent attacks of tracheobronchitis	No demonstrable change	No demonstrable change	Pyelitis following respiratory tract infection				JANUA gro Deve
					Several respiratory tract infections	Liver enlarged				FEBRU
INACTIVE although there is		mechanical								Origi abdo indi infl diti deaf as c tion cont of a deat of a trea medi
			COMPLAINTS OF GASTRO-INTESTINAL TRACT		CONTINUE AS BEFORE		NO DEMONSTRABLE CHANGE IN			
							CONDITION - BED CONSTANTLY			
							EXCEPT FOR OCCASIONALLY			
							SITTING UP IN CHAIR			
	NOVEMBER returned to Robert Brigham Hospital. No demonstrable change in condition from that present in 1918									
									Blood pressure slight rise,-160-170/80-90	
							SUBNORMAL TEMPERATURE CHART THROUGHOUT		EXCEPT WITH INFECTION	
R.B.C AND	ALBUMIN:		SPECIFIC GRAVITY FIXED BETWEEN		1014 A		ND 1022.	BLOOD PRESSURE AVERAGE		

27th year	28th year	29th year	30th year	DEATH:
46-47 years (1929)	47-48 years (1930)	48-49 years (1931)	49-50 years (1932)	AGE: 49 years
FEBRUARY: Improvement APRIL: OPERATION:Double ethmoidal exenteration Right frontal sinus; Excision tonsillar tab MAY: Occasional complaint of vague lower chest and upper abdominal discomfort and pain. Joints about the same. Good function; lessening discomfort. Discharged. LABORATORY work essentially normal except; low vital capacity. NPN 41.3 Renal function 59% Blood calcium 9.6 " Phos. 9.7 Rest of year up and about at home; doing housework. No great functional handicap. Occasional mild flare-up in joints. Some slow increase in deformity of fingers	Continued in good condition this year, with her usual intermittent attacks of bronchitis. DECEMBER: Readmitted to Robert Brigham Hospital with swollen, flexed tender and painful metacarpophalangeal joints left hand.	FEBRUARY:Improved; up and about ward. Chief complaint; constipation. APRIL: Discharged. Total duration of flare-up, 3 months. Occasional upsets; remissions and relapses in joint symptoms. JULY: Flare-up of antrum. Small polypi and granulations in region of ethmoidal sinuses; mild pharyngitis with increased shortness of breath. OCTOBER: Another attack of bronchitis. DECEMBER: Paresthesia skin;small black and red marks under skin. B.P. 140/100;pulse 96 HEART action regular but labored,rate 84-96 Bubbles in lungs. Complaint of tremendous weakness and constant fatigue Blood count normal. Blood uric acid 3.6	JANUARY: Sore throat, followed by chest involvement;cough;blood tinged sputum;substernal soreness. No joint flare-up X-RAY:Peribronchial fibrosis upper left lobe. Heart shadow normal size. Increased difficulty at night in breathing. FEBRUARY 5 to MARCH 17, hospital,during which time asthmatic attack cleared up. Fine wheezing remained. Flare-up,short duration,right hip;some lameness knees and hands Sputa negative for T.B. MARCH Chest infection MAY Chest infection; flare up knee JUNE: Subacute pneumonitis JULY: Heart sounds poor quality; emotionally upset AUGUST: Acute flare-up; orthopnea,dyspnea; cough; wheezing X-RAY:Increased density aorta;enlargement heart (This occurred during 6 month period) Auricular Fibrillation appeared;lungs showed moist fine rales. Temporary hemiplegia. Ups and downs, but steady downward course with repeated bombarding body with emboli; mental changes. Fever last 4 months. DECEMBER: DIED.	DURATION ARTHRITIS: 29 years DIAGNOSES: Chronic arthritis, mixed type Arteriosclerosis: Auricular Fibrillation; Cerebral hemorrhage P.M. DIAGNOSES: Ante mortem thrombus right and left auricles; Infarcts brain. Vegetative Endocarditis: Hypertrophy Heart Multiple recent Infarcts Lungs: Hydrothorax, bilateral; Multiple healed Infarcts Spleen; Edema Extremities: Arthritis Deformans. Arteriosclerosis, intimal type: Chronic passive congestion lungs, liver and spleen Healed salpingo-oophorectomy right Leiomyoma uteri Cerebral softening SUMMARY: Involved: Joints Cardiocirculatory G.U. Tract ADDITIONAL LOAD: ? Gonorrhea Antra Tonsils Teeth

100%

75%

50%

25%

0

TYPICAL LIFE-COURSE D

2nd year	3rd year	4th year	5th year	6th year	7th year	8th year	9th year	DEATH:
42-43 years (1921)	43-44 years (1922)	44-45 years (1923)	45-46 years (1924)	46-47 years (1925)	47-48 years (1926)	48-49 years (1927)	49-50 years (1928)	AGE: 49 years
Low backache. Periods of remission and relapse but trend downward. Symptoms worse in damp weather. Walking difficult Slow steady increase in arthritic involvement and disability.	JANUARY: Pain through ribs APRIL: Aching in cervical spine JULY Admitted Robert Brigham Hospital Not bed ridden but walking very difficult. Chief complaint: Pain and weakness in joints; headache; blurring vision; earache; dyspnea on exertion; constipation; ? night sweats; dryness in throat. P.E. TEETH:Plates TONSILS present LUNGS: Some dulness middle angle scapula to bases with increased tactile and vocal fremitus; prolonged inspiration SPINE: Left dorsolumbar curve. JOINTS: Elbows, wrists, hands and knees swollen and limited motion B.P. 150/92 Blood normal NOVEMBER: Flare up right knee DECEMBER: Flare up left wrist CONSTANT EVENING	JANUARY through MARCH: Acute joint flare-up continued; then some subsiding of symptoms NOVEMBER: OPERATION: Tonsillectomy: Right radical antrum DECEMBER: Condition definitely worse than a year ago FEVER 99° - 100°	APRIL: X-RAY: Thinning of cartilages; thickening synovia; soft tissue swelling AUGUST: X-RAY: Destruction of cartilage of wrists; regenerative changes LOW Sugar Tolerance Fairly constant complaint of pain Less active GRADUAL AND FAIRLY Evening fever continues; Slightly less high this year	JANUARY: X-RAY: Knees thinning of cartilage; atrophy of bone; slight evidence of regeneration Joints this year stiffer; less motion. Arthritic process continues active. Evening fever continues Definitely higher elevations this year; 99.5°, often 100° or 101°	Increasing pain and deformity Arthritic process continues active X-RAY: Sacroiliac joints beginning to fuse; erosion of bone about joints;definite increase in arthritic process with more destruction; generalized bone atrophy, destruction and some ankylosis; mushrooming of some of joints STEADY LOSS OF WEIGHT 12 pounds Evening fever almost constant; 99°- 101°	JANUARY: Pain across chest Bedridden; or occasionally up in chair. Condition nearly helpless. Knees and elbows permanently flexed. Skin very tense shiny and atrophic APRIL: Discharged against advice OCTOBER: Admitted to another hospital; condition unchanged. No carcinoma recognized	APRIL: Admitted to another hospital; died same day. Carcinoma of breast with metastasis.	DURATION: 8 years DIAGNOSES: Chronic arthritis, Type 1 Hypertensive Heart Disease, early Pulmonary Tuberculosis (?) Carcinoma of breast with metastasis SUMMARY: Involved: Bones; joints Cardiocirculatory Respiratory ? ADDED LOAD: Tonsils Antra Tuberculosis ? Carcinoma

100%

75%

50%

25%

0

26th year	DEATH:
74-75 years (1930)	AGE: 73 years
JANUARY: Gradually growing weaker. Developed pneumonia FEBRUARY: DIED Original complaints,- abdominal pain, indigestion, cough, inflammatory condition of eyes, deafness, as well as complete functional disability, continued from day of admission to death, in spite of all forms of treatment and medication.	DURATION: 25 years DIAGNOSES: Bronchopneumonia Chronic atrophic Arthritis Chronic Pyelitis Arteriosclerosis, generalized Pulmonary Tuberculosis Chronic Nephritis P.M.DIAGNOSES: Pulmonary tuberculosis Adhesive Pleurisy Anthracosis with pulmonary fibrosis. Congestion liver Cystitis Pyelonephritis, left Pyelonephrosis, left Arteriosclerosic Nephritis Chronic Progressive Nephritis Atrophic Arthritis SUMMARY: Involved: Joints and bones Cardiocirculatory Kidneys Eyes Ears ADDITIONAL LOAD: Tuberculosis ? Tonsils ? Lead Poisoning

100%

75%

50%

25%

0

FEMALE	Gastro-Intestinal Volvulus	42	54	12	Mixed		Arteriosclerosis Cardiac dilatation acute: Brown atrophy	None Recorded	Involuted uterus: Sclerosed ovaries Chronic cystic endocervicitis: Chronic glomerular nephritis	None Recorded	Volvulus Sigmoid colon	44	Pleurisy Bronchiectasis: Congestion Fibrosis				Fibroid	Atrophic: Congested			
MALE	Nephritis	29	42	13	Str. Marie	Atrophic Arthritis, Strumpel Marie	Arteriosclerosis	40	Chronic nephritis: Amyloidosis kidney	34	None	39	Hydrothorax	37	Pulmonary Healed		X		Amyloidosis	Localized thickening arterioles	Amyloidosis	Bronchopneumonia		
MALE	Pneumonia on Hypertensive Heart Disease	23	63	40	2		Arteriosclerosis: H & D heart: Syphilitic aortitis	56			None	56	Healed fibrous pleuritis	36					Cirrhosis, alcoholic			Lobar Pneumonia		
LIFE COURSE C (6)																								
FEMALE	Hypertensive Heart Disease	31	53	22	1	Chronic Atrophic Arthritis	Chronic myocarditis: Chronic inflammatory adhesive pericarditis	49	Chronic nephritis	34			Chronic Sacculated Pleuritis	11	Pulmonary	?			Perihepatitis					
MALE	Pneumonia on Rheumatic Heart Disease	25	38	13	1	Chronic Arthritis: No active destruction done.	Chronic myocarditis	29	Chronic nephritis with edema of cavities and skin	35			Pleuritis Hydrothorax	None Recorded								Bronchopneumonia		
MALE	Bronchopneumonia	48	73	25	1	Atrophic Arthritis	Progressive arteriosclerosis, chronic	None Recorded	Cystitis: Chronic Pyelonephritis: Pyelonephrosis: Hydro-ureter	58	None	58	Adhesive Pleurisy: Pulmonary Fibrosis Asthracosis	64	Lungs				Congestion					
MALE	Pneumonia	28	55	27	1	Chronic Infectious Arthritis (Knee)							Chronic fibrous Pleuritis	45	Lungs, healed									
MALE	Gastric ulcer with Sepsis	45	62	17	1	General atrophy and deformity	Myocarditis Thrombosis aorta	None Recorded	Chronic Pyelonephrosis	None Recorded	Duodenal ulcer	55	Emphysema	None Recorded	Lungs and pleura, healed									
FEMALE	Pneumonia	47	72	25	1	Atrophic Arthritis	Adhesive Pericarditis	None Recorded			Adhesive Peritonitis	None Recorded												
LIFE COURSE D (5)																								
FEMALE	Pneumonia	56	59	3	Mixed	Hypertrophic Arthritis with erosion	Arteriosclerosis	29	Cirrhosis Kidney Chronic cystitis Endometritis Cystic Ovaries	59			Adherent pleurae: Emphysema	None Recorded				Splenitis	Cirrhosis			Lobar Pneumonia		
MALE	Staphylococcus Bacteremia	81	81	10	Str. Marie	Chronic Arthritis: No active Infection	Myocarditis	None Recorded	Acute and chronic Prostatitis: Hypertrophy Prostate: Acute toxic Nephritis	29								Acute tumor	Hepatomegaly	Acute Infectious Pancreatitis		Bronchopneumonia: Staphylococcus: Peritonitis: Infectious Pancreatitis		
MALE	Pneumonia on Thoracic Aneurysm	64	66	2	2	Hypertrophic Arthritis Spine	Arteriosclerosis Fusiform & dissecting aneurysm aorta: Syphilitic aortitis	60	Hypertrophy Prostate	64	None	64	Healed fibrous Pleurisy							Hemorrhagic necrosis		Lobar Pneumonia		
FEMALE	Syphilitic Aortitis with Nephritis	56	65	9	2	Red Marrow in long bones	Arteriosclerosis Syphilitic aortitis	62	Chronic nephritis	60	Atrophy of intestines with numerous scars	None Recorded	Hypostatic Congestion	49	Lungs, both bases old									
MALE	Cardiosclerosis	63	71	8	2		Arteriosclerosis H & D heart	69	Chronic nephritis	55	None	70		69	Lungs, Obsolete							Hypostatic Pneumonia		

TO SUMMARIZE THE ABOVE CHART ONE MAY SAY THAT IRRESPECTIVE OF THE TYPE OF ARTHRITIS DESCRIBED, THE PATHOLOGICAL CHANGES ARE COMPARABLE, OR ALMOST IDENTICAL, WITH THE CHANGES FOUND IN SIMILAR GROUPS WHO HAVE NO JOINT MANIFESTATIONS.

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ANALYSIS OF 95 DEAD ARTHRITICS

RELATIONSHIP BETWEEN ARTHRITIS AND OTHER SYSTEMIC INVOLVEMENTS

AND

DIVISION OF GROUP BY

"LIFE-COURSE"

*PAST HISTORY
**PRESENT ILLNESS

| SEX | FAMILY HISTORY 'TISSUE' | FAMILY HISTORY 'ARTHRITIC' | CAUSE OF DEATH | POST MORTEM | ARTHRITIC SYNDROME TYPE | AGE ONSET | AGE DEATH | DURATION | JOINT INVOLVEMENT BILATERAL | JOINT INVOLVEMENT MULTIPLE | OPERATIONS | 'OTHER SYSTEMS CHRONICALLY INVOLVED and 'ATIENT'S AGE at TIME of RECOGNIZED INVOLVEMENT' CARDIO-CIRCULATORY SYSTEM | AGE | GENITO-URINARY SYSTEM | AGE | GASTRO-INTESTINAL TRACT | AGE | BLOOD | AGE | TISSUE (SKIN) LOOSE SKIN | AGE | ENDOCRINAL | AGE | RESPIRATORY | AGE | MUSCULO-SKELETAL | AGE | OPERATIONS | FOCI OF INFECTION and ADDITIONAL LOADS TONSILS | F. | B.P. | F. | GALL BLADDER | F. | APPENDIX | F. | ANEMIA | F. | TEETH | F. | P. | OPERATION | AGE | CLINICAL DISEASE ENTITIES PAST HISTORY | PRESENT ILLNESS | ABNORMAL LABORATORY FINDINGS |
|---|---|---

whom attention has been focused primarily in this series of papers, and on whom the medical profession should centre its most earnest attention.

Reproduction of the working charts seems the briefest way of explaining the findings in this study. Multiple systemic involvement accompanying arthritis was proved beyond doubt. In fact, autopsy showed in many cases even greater body change than had been manifested clinically. On the other hand, one case whose chief complaint throughout fifteen years of observation had been of the gastro-intestinal tract showed at autopsy a perfectly normal tract. Obviously his symptoms were due to functional and not pathological change.

A summary of the working chart accompanies this article.

COMMENT

Course A averaged the longest duration of life after onset of arthritis. The patients in this group showed no signs of arthritic activity after the subsidence of the first attack during the greater part of their remaining life.

Course C averaged the second longest life line after onset of joint manifestations. This is probably explainable on the basis of removal from the hazards of life.

The greatest contrast lies between Course A and Course D.

Of the 95 patients studied 5 or 5 per cent, followed Course A: 51, or 54 per cent, Course B: 13, or 14 per cent, Course C: and 26, or 27 per cent, Course D. As has been said, they fell into these groups apparently without rhyme or reason. As regards the various systemic involvements, no outstanding fact was shown except the presence of general body imbalance. In the majority of cases the arthritic signs and symptoms antedated those of other systems.

Actually, except for the definite fact of general body involvement accompanying arthritis only one definite observation is apparent, that is the *lack* of any one common etiologic factor in the group of arthritics studied.

CONCLUSION

This paper is one of a series which has resulted from two years of concentrated work on a survey of chronic disease. In this serial study, an analysis, from a clinical point of view, has been made of arthritis and its relationship to dysfunction of various body systems, to certain disease entities, and to other additional loads which the arthritic may be carrying. The relationship between arthritis and sugar tolerance and arteriosclerosis has been dealt with in the two preceding papers. (At this stage of our study, emphasis cannot be laid too strongly on the prominent part that disturbance of the endocrinal-neurological systems plays in the arthritic.) This article represents an attempt to picture the life course of chronic disease in a group of dead arthritics. It is an analytical study in which one may read discouragement or encouragement, but in which the authors read encouragement.

All chronic diseases have of course many points of similarity, but perhaps the most marked are those existing between arthritis and tuberculosis, syphilis and leprosy. In each of these there is a variety of location selected by the disease for attack; there is a variable period of time the disease may lie latent before recognition; and there is a variable span of life after recognition. In each disease there is a constant inconstancy and lack of reason in the clinical manifestations, other than individual receptivity. The chief difference between arthritis and these other diseases is unfortunately a most vital one, knowledge of the specific agent on the one hand and ignorance on the other. However, even in those diseases whose etiologic agent is known there is no specific, one-hundred per cent prophylaxis or cure, and the surest method of attack is one of rest and general upbuilding. For some years arthritis has been treated along general systemic lines, ameliorative, supportive, corrective and preventive; lightening the load from one or another system, and this program should certainly still be followed. All these things in turn may affect physically the joint involvement. Until the arthritic agent or agents are found, the need for concentrated, tireless search for the actual cause of arthritis remains paramount. However, it seems an encouraging point that from these completed cycles of life one may learn the probable life course of the arthritic, and with a more comprehensive knowledge one may be able to alter and better this potential course, to raise those in Course C and Course D to Course B, and those in Course B to Course A.

As the Survey progresses, and after the living arthritics have been charted along similar lines over a comparable period of time, certain definite leads may appear indicating more specific, practical therapeutic measures. This is our hope, and if it is realized then we may truly say "The Dead Teach the Living."

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VERMONT STATE MEDICAL SOCIETY

NEUROFIBROMATOSIS IN CHILDREN: REPORT OF TWO CASES*

BY COLIN C. STEWART, M.D.†

ALTHOUGH multiple nerve tumors had been described a number of times previously, Virchow[9] in 1863 was the first to show that they were not true neuromas, but arose from the fibrous tissue sheaths of nerves. In 1882 von Recklinghausen[10] demonstrated that what had before been considered a number of diverse processes was in reality one disease, which has since generally been known by his name.

Several attempts have been made to classify these various forms of the disease, but a majority of the terms have been merely descriptive of one or more of its many features. Thomson[8] in an exhaustive monograph published in 1900, listed six varieties which may be found singly or, more often, in combination. Thus there may be a diffuse and generalized overgrowth of the connective tissue sheaths of nerve trunks. Further observation has shown that what were thought to be independent tumors along these nerves are really but local exaggerations of this diffuse fibromatosis.

A second form, the plexiform neuroma, is the result of a localized fibromatosis following the distribution of one or more contiguous nerves or of a nerve plexus. The tumors, which involve mainly cutaneous and subcutaneous nerves, consist of tortuous, lumpy, fibromatous cords held together by a loose, fatty connective tissue. Seventy per cent are found on the head and neck. There is usually a capsule, but when this is absent, cords of fibromatous tissue may penetrate muscles. The overlying skin may appear normal, and yet show microscopically extensive neurofibromatosis. This form is usually associated with generalized fibromatosis.

A third type, sometimes called molluscum fibrosum, presents usually numerous cutaneous neurofibromas. These occur as small soft papillomatous tumors or as flatter subcutaneous swellings, arising from fine cutaneous nerve filaments[10]. The scalp, dorsal aspect of the trunk and lumbosacral region are the sites of predilection; they are infrequent on the forearms and legs. The smaller ones are quite uniform in consistence, others may be lobulated and others again are made up of convoluted cords, movable on each other. The skin may also be the seat of extensive fibromatosis in relation to the terminal distribution of the cutaneous nerves, without visible evidence on the surface.

There may be a pronounced diffuse overgrowth of the skin and subcutaneous tissues in some particular region of the body, so extensive as to deserve the name "elephantiasis nervorum". The overlying skin may be pigmented and greatly thickened. Transition forms between this and the plexiform neuromas have been described. Like the latter, this type is frequently found on the head, where it can become so disfiguring that operative removal is necessary[3].

Scattered areas of pigmented skin, varying from freckles to spots several centimeters in diameter are seen in conjunction with other manifestation of von Recklinghausen's disease. These are commonly referred to as café au lait patches. An abortive form of the disease occurs, in which these spots are the only presenting signs. The nature of the affection may be discovered in such cases through their relationship to more typical cases.

Secondary malignant neuromas occur in 17 per cent of cases[8]. Sarcoma develops frequently after trauma, including operation, especially if removal is incomplete. There is slight tendency to metastasize, but early and persistent recurrences after surgical removal make the mortality high.

Few symptoms are directly attributable to the neurofibromas. Motor and sensory disturbances are rare, doubtless because the nerve fibers, though sometimes widely separated by fibromatous tissue, show only slight and inconstant changes. Pain of a neuralgic character occurs infrequently. Occasionally in the severe cases there is cachexia, thought to be due to involvement of the sympathetic nerves, which is frequently encountered. The cranial nerves show fibromatous changes in two-thirds of the recorded cases. Although none is exempt, the vagus is most often affected.

In connection with, and dependent upon the nerve tumors, there are frequently other manifestations of this widespread malady. X-ray studies show cyst-like areas in the bones of a considerable percentage of cases. These are not true cysts, but fibromatous tumors beneath the periosteum. Overgrowth of bones occurs in the forms with elephantiasis; but if the epiphyses are involved in childhood, the limb may be normally short. Scoliosis is frequent, due either to direct involvement of the spine, or secondary to an inequality in the length of the lower extremities[5]. Tumors occurring within the spinal canal or in the brain may give symptoms due to pressure on surrounding structures. Kass[4] reports the case of a boy having extensive neuro-

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fibromatosis of the bladder; but visceral involvement is uncommon.

There are also abnormalities associated with, but not necessarily caused by, the nerve lesions themselves. Mental and psychic alterations may be regarded as cardinal features of the disease[2]. Feeblemindedness was found in 7.8 per cent of one series of cases[7] and epilepsy is frequent. There may be structural changes, as focal gliosis or cyst formation in the brain, to account for these symptoms. Vascular nevi, ichthyosis, congenital cataracts and other defects are described.

Symptoms suggestive of various forms of glandular dysfunction are common[2, 8]. The patients are often below average size, or sexually underdeveloped. Adrenal changes are suggested by the pigmentation and have been described at necropsy; while acromegaly and myxedema occur in some cases. Since the endocrine disturbance has been observed in a number of cases before the neurofibromatosis, it is usually felt that they are separate manifestations of a common causative factor, rather than dependent one on the other.

The cause of von Recklinghausen's disease is generally conceded to be a developmental anomaly of either the ectoderm or mesoderm or both. Penfield and Young[6] suggest that a defect in the nervous system is in some way capable of producing irritation of adjacent tissues, resulting in hyperplasia of the cells susceptible to stimulation, and secondarily in neoplastic changes. This defect is inherited as a dominant factor.

Preiser and Davenport found neurofibromatosis in 43.5 per cent of 115 children who had one parent affected. Not only the disease, but apparently also the localization of the lesions can be inherited[7]. A remarkable illustration of this is furnished by Gardner and Frazier[1], who report a family having bilateral deafness due to neurofibromatosis of the acoustic nerve in 38 members.

The first case, C. T., is a colored girl, aged 16, who has had molluscous skin tumors since she was a baby. Two older sisters, one younger brother and a younger sister are normal; one brother died in infancy of meningitis. The patient is tall, with large features, and, compared with her well-built brothers and sisters, poor posture and general appearance. She is awkward in fine motions, and is considered "queer" by her teachers. She is lighter colored than the others, with several patches of deeper pigmentation. There are a hundred or more small soft projecting skin fibromas, most numerous on her back and sides, and a few of the flat subcutaneous tumors as well. There are no tumors of nerve trunks apparent.

The second case, J. B., is a boy of 12, whose parents and two brothers and sisters are said to be well. He was brought to the hospital for tonsillectomy. On a previous admission a mass the size of an egg had been removed from his neck, the preoperative diagnosis being Hodgkin's disease. The pathologic diagnosis was neurofibroma. On examination he was found to be somewhat underdeveloped, and distinctly dull mentally. His skin was thick, dry and scaly, a typical ichthyosis. There were several café au lait patches on his back and thighs and a few small soft subcutaneous tumors. There was considerable swelling of the subcutaneous tissue of the neck, more on the side from which the piece had been removed. Irregular cord-like strands could be felt within this tumor, which was not tender.

COMMENT

The first patient is a typical case of cutaneous neurofibromatosis or molluscum fibrosum, with, in addition, the café au lait spots usually associated with it. Her coarse features, large mouth, large hands and feet and height, greater than her three sisters, suggest a mild acromegaly. The mental signs are not pronounced enough for a definite diagnosis, but fit in with the other features of von Recklinghausen's disease.

The coexistence of ichthyosis and neurofibromatosis in the second case emphasizes again the probability of a defect in the germ plasm controlling neuro-cutaneous development. This case also exemplifies a most important point, the possible value of a few cutaneous neurofibromas or café au lait patches in indicating the true nature of a plexiform neuroma. These tumors by themselves might be mistaken for lymphangiomas, Hodgkin's disease, etc. The diagnosis should be made without biopsy whenever possible, for, while surgical removal cannot always be avoided, the possibility of precipitating a malignant change should be borne in mind.

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DISCUSSION

PRESIDENT ALLEN: I am going to say at the beginning of this discussion that if anyone has seen similar cases, we should like to have him report it.

DR. CRAMPTON: I had one, in clinic work, in Pittsfield. He had some 200 lesions, probably, on the face and neck and back of the scalp. The majority of them were a half to one inch in diameter, but

one on the buttocks was the pendulated type, and we thought somewhat of removing it, but didn't.

DR. BUNCE: I served as internist at the New York Skin and Cancer Hospital several years ago, and I saw two cases, and both of them were Negroes. I would like to ask Dr. Stewart if this condition is found more frequently in Negroes?

DR. STEWART: In my cases one was white, the other a Negress.

DR. T. J. ALLEN, Brandon: The experience I have had is in a middle-aged woman who has the physical changes of acromegaly. She had hundreds of the cutaneous tumors of different sizes, from very small to those perhaps half an inch. She was committed as a mental defective, but as a matter of fact she is physically rather than mentally defective. Her I. Q. is 85 or so, which shows she is not too limited. She has no motor or sensory signs. I was interested in remarks made in connection with apparent instances of mental defects, and other neurologic conditions associated with neurofibromatosis. In its inherited nature, as I understand it, the speaker suggested that many of these cases are those of familial transmission, apparently.

DR. LYMAN ALLEN, Burlington: I have seen one case in an adult, a rather small, poorly developed man, with a piping voice and rather a kindly disposition, but mentally well; a laborer who for years had worked on the farm. The proprietor said he was faithful, but slow mentally. I know nothing about the family history, and am not positive of my diagnosis, but that is the only thing I think it could be.

DR. JOHNSON: Are the majority of those cases in mental, or feebleminded institutions? Would Dr. Allen tell us how many cases he has seen at Brandon?

DR. T. J. ALLEN, Brandon: This is the only case I have observed, and in this particular individual I do not consider her mentally defective, but she is physically defective in several ways, and I should have added that she is a member of a quite outstanding family, intellectually. I have not had any of these cutaneous tumors in any of the other cases I have seen at Brandon.

DR. STEWART: As in most congenital conditions, one naturally expects to find cases of neurofibromatosis in children, but the number reported has been rather small. In most of the childhood cases, neurofibromas were first noticed during the second and third years. Development at adolescence is also said to be frequent.

Dr. Bunce asked about the incidence in Negroes. The one time I have seen this mentioned in the literature it was said to be rare in Negroes, but the statement was not supported by statistics. We must remember that many so-called Negroes have both black and white ancestors, and it is difficult to say which race has transmitted a given condition, so we really ought not to talk about inheritance in one race or another, when we are dealing with a mixed race.

In connection with the mental symptoms, the structural changes found in the brain at necropsy are of interest. A patient of ours recently died of sarcoma, on the basis of neurofibromatosis. There were areas of gliosis and one cyst in his brain, although there had not been any mental symptoms. Attention has been called to a possible relationship of von Recklinghausen's disease to other syndromes, in which various skin changes are associated with degenerative brain lesions, and often with epilepsy or feeblemindedness as well. The group with tuberous sclerosis of the brain and adenoma sebaceum of the face is an example. In these other neurocutaneous syndromes, a few neurofibromas or café au lait patches are occasionally seen.

Dr. Johnson asked about inheritance. Unfortunately, I have had no opportunity to examine all the relatives of my patients. The first patient's paternal uncle and his numerous children are normal, but I have only the report that none of her mother's family are affected. The boy's family I have not been able to examine. The reliable statistics on heredity in this condition we owe to a few authors who have studied large numbers of cases and their families very thoroughly. When all of the relatives are carefully examined, nearly 50 per cent of the second generation show evidences of the disease. It is easy to overlook some cases, such as a boy reported recently who presented only a few pigmented spots, but on x-ray study several bone cysts were found, presumably associated with internal neurofibromatosis.

MISCELLANY

VERMONT DEPARTMENT OF PUBLIC HEALTH

NOVEMBER, 1933

The incidence of communicable diseases reported to the State Department of Public Health during November is as follows: chicken pox 278, diphtheria 12, measles 161, mumps 23, scarlet fever 52, poliomyelitis 3, tuberculosis 3 and whooping cough 210.

The Laboratory of Hygiene report a total of 1705 examinations made in November, classified in the following manner:

Examinations for diphtheria bacilli	310
" " Widal Reaction of typhoid fever	20
" " undulant fever	24
" " gonococci in pus	164
" " tubercle bacilli	247
" " syphilis	470
" of water, chemical and bacteriological	92
" " water, bacteriological	180
" " milk, market	119
" " milk, submitted for chemical only	5
" " foods	9
" " drugs	2
" for the courts, autopsies	1
" " evidence of rabies	1
Miscellaneous	47
Autopsies to complete death returns	1

Thirty-six cases of gonorrhea and fourteen cases of syphilis were reported to the Division of Communicable Diseases in November. Three hundred and sixty-four Wassermann outfits and 241 gonorrheal slides were distributed.

Ten thousand copies of the Modern Health Crusaders have been published and mailed by the Di-

vision of Tuberculosis, and several talks on health given in village rural schools.

Approximately 150 patients were seen by the nurses in the Division of Poliomyelitis After-Care, 146 of these being home visits. Three patients were admitted to the Children's Hospital for treatment and one to the Audubon hospital. Eighteen new pieces of apparatus were fitted and six pieces repaired. The vocational worker of this division reports sales made to the amounts of $74.45.

The State Advisory Nurses visited several towns in the state arranging for health work connected with county health movements, conferences with Health Committees and assisting Home Demonstration Agents. In this Division 145 bulletins and 255 notifications of birth registrations were sent out.

BOSTON MENTAL HYGIENE SURVEY

REPORT OF PROGRESS OF THE EXECUTIVE COMMITTEE

With the encouragement of the Massachusetts Society for Mental Hygiene a large committee of executives and others, representatives of hospitals, clinics, and social agencies in the mental hygiene field, was created for the purpose of exploring further the conditions noted in the Report of the Boston Mental Hygiene Survey, with the hope that this committee might recommend ways in which the difficulties referred to could be corrected.

An Executive Committee was invested with the full authority of the whole committee and it has had many meetings since it began to function early in 1932. It has had many contacts with social agencies, with the expectation that out of such contacts would come a greater knowledge on the part of our Committee as to the needs of individual social workers, for it is to this problem that the Executive Committee has devoted most of its time.

It is the belief of the Committee that one of the chief lacks in Boston is an up-to-date mental hygiene training for social workers in service. The Committee has found that there is clearly an increasing desire on the part of social workers to secure more mental hygiene training.

Tentative plans were worked out for a four weeks' institute in the spring of 1933, but the financial situation in which the agencies and individual workers found themselves was such that the plan had to be postponed. A subcommittee is now at work on a substitute for the institute. — *Bulletin, Massachusetts Society for Mental Hygiene*, November, 1933.

"VARIATION" CLAUSE INTERPRETED

The so-called "variation" clause in the provisions of the Federal food and drugs act which deals with U. S. Pharmacopoeial and National Formulary drugs applies only to differences in the strength, quality or purity of the products, according to W. G. Campbell, Chief, Federal Food and Drug Administration. The clause does not permit the use of ingredients differing from those prescribed by the definition or formula.

In a recent decision of the U. S. Circuit Court of Appeals for the Second Circuit in the case of the U. S. vs. Harry Lesser, et al, it was held that noncompliance with the U. S. Pharmacopoeial standards could be established not only by the methods of analysis prescribed by the U. S. P., but also by any other logical and convincing means.

"An example of what must be considered a violation of the food and drug law under this principle," said Mr. Campbell, "is a product labeled as milk of magnesia manufactured from ingredients other than those stated in the monograph for milk of magnesia in the United States Pharmacopoeia."—*Bulletin, Department of Agriculture.*

HOFFMAN CANCER LIBRARY

Dr. Frederick L. Hoffman of Wellesley Hills, Massachusetts, has made an outright gift, in behalf of himself and the Prudential Insurance Company, of his accumulation of cancer books, papers and records to the Cancer Research Laboratory of the University of Pennsylvania. This collection in the future will be known as the Hoffman Cancer Library.

Dr. Hoffman will move to Melrose Park, Philadelphia, and his future office will be in the Cancer Research Laboratory, 133 South 36th Street, Philadelphia. At present he is concentrating upon cancer in relation to diet and nutrition, concerning which he expects to publish an extended report in the near future.

NEW YORK ACADEMY OF MEDICINE

Dr. Charles Macfie Campbell, professor of Psychiatry at the Harvard Medical School and medical director of the Boston Psychopathic Hospital, has been selected to deliver the 1934 series of Thomas W. Salmon Memorial Lectures.

His lectures, to be delivered on Friday evenings, April 13, 20 and 27, will deal with "Trends in Psychiatry."

1933 A YEAR OF GOOD HEALTH

According to a report of the Metropolitan Life Insurance Company, the United States had in 1933 what was probably the best health record "of all time". The signs, moreover, are excellent for 1934, although the year's health depends in large measure on our good fortune in escaping epidemics. The chances, are, however, that we shall not suffer an influenza epidemic of any proportion in 1934, the last major influenza outbreak having occurred late in 1932 and early in 1933.

CASE RECORDS
of the
MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

EDITED BY RICHARD C. CABOT, M.D.
F. M. PAINTER, A.B., ASSISTANT EDITOR

CASE 20031

PRESENTATION OF CASE

A thirty-nine year old white married American teacher entered with the complaint of headaches, nausea and vomiting of three weeks' duration.

Fourteen months before admission he developed what appeared to be grippe, with fever and soreness of his muscles. This lasted three to four days, following which he complained of numbness of the right side of his face accompanied by tingling. Two months later his right eye began to bother him and he complained of double vision. An oculist told him that his trouble could not be remedied by glasses. His right eye was not so efficient as his left. He continually bit the inner side of his right cheek. He had slight headaches but no nausea, vomiting, convulsions or weakness of any other muscles. He complained of a tense feeling in the region of the right temple which was worse upon moving his head. Shortly afterward his face became completely paralyzed on the right. A neurologist made a diagnosis of brain tumor and x-ray treatment was given, following which all paralysis cleared up. Five months later, six months before admission, his headaches recurred. This time he had six or seven attacks of unconsciousness. These attacks occurred with no aura, convulsions or incontinence. He would simply awake to find his head on his desk. He had an attack three months before admission, but had had none since. Three months before entry he began to have severe frontal headaches and double vision. He also vomited a few times. The headaches grew worse and during the past month had been associated with nausea and non-projectile vomiting. For the past three weeks he had been spitting up clots of blood which he believed came from the back of his throat. He also noticed a small amount of blood in his handkerchief after blowing his nose. For the past eight months he had had deafness in his right ear, recently increased in severity. For the past month he had staggered slightly to either side. He had lost about ten pounds in weight. There had also been moderate loss in strength.

His family and marital histories are irrelevant.

The only positive finding in his past history was that he had failed an army test in 1917 because of Bright's disease. There were no symptoms however.

Physical examination showed a well developed and well nourished man complaining of headache. His mouth contained small beads of bloody mucus. No bleeding points were seen however. Over the sternum in the region of the second rib was an elevated firm adherent mass 3.5 by 4 centimeters.

Neurological examination on the day following admission was as follows. The left optic disk was slightly blurred. The right was normal. Both disks were probably within normal limits, but there seemed to be a definite difference on the two sides. The right pupil was slightly irregular, larger than the left, and reacted very slightly to light. The left pupil reacted fairly well. The right external rectus was weak, but there was some outward movement of the right eye. There was complete paralysis of the left external rectus. Pin and touch sensations were impaired on the right side of the face. There was a moderate right facial weakness of the peripheral type. His hearing was less distinct on the right side. On the right bone conduction was greater than air conduction. On the left air conduction was greater than bone conduction. The palate was in the midline. His speech was not nasal. His tongue showed no atrophy, although there was a questionable deviation to the left. There was good strength in both arms and legs. There was no intention tremor or unsteadiness. The biceps, supinators, knee-jerks, ankle-jerks and abdominal reflexes were present on both sides, although stronger on the left. The plantars pointed downward.

X-ray examination showed considerable decalcification of the dorsum, sella, posterior clinoid, and the floor of the sella. There was also some irregularity of the posterior surface of the dorsum. The sella turcica was normal in size and shape. There was calcification just posterior to the clinoids, probably in the ligaments passing to the posterior clinoids. The pineal was calcified and lay in its normal position. There was also calcification in the choroid plexus. In the posterior portion of the left occipital bone there was an irregular area, 1.5 centimeters, of diminished density. The convolutional markings were not unusually prominent. The vascular channels appeared normal. A chest film was negative. Another film four days later showed an area of rarefaction in the left parietal bone. The vertebral column and pelvis showed no evidence of disease.

Examination of the urine showed a specific gravity of 1.024. There was a very slight trace of albumin; no sugar or bile. Examination of the blood showed a red cell count of 3,000,000, hemoglobin 65 per cent. The white cell count

was 3,350, with 68 per cent polymorphonuclears. The Hinton test was negative.

A lumbar puncture showed clear colorless fluid. The initial pressure was 180. The dynamics were normal. The ammonium sulphate and alcohol tests were positive. The Wassermann was negative. There were 93 red blood cells (fresh), no white blood cells. The total protein was 95 milligrams, the colloidal gold 5555555554, sugar 105 milligrams.

On the fourth day examination of the nasopharynx showed a small bleeding granular mass on the right side just lateral to the right eustachian orifice.

On the fifth day a biopsy from the sternum was taken. There was a large amount of bleeding from the site of this biopsy.

Differential Diagnosis

Dr. J. H. Means: The symptoms in this case from the very beginning point toward the cranial nerves. We have, to be sure, what was called grippe at the onset, but this was immediately followed by numbness and tingling of the right side of the face, suggesting involvement of the right trigeminal nerve. Two months later he complained of double vision, presumably due to some sort of ophthalmoplegia. Also at this time he began to bite the inner side of his right cheek, which I take to be further evidence of right trigeminal involvement. The significance of headache without other general symptoms I cannot undertake to evaluate. The feeling of tenseness in the region of his right temple might be indication of a lesion in that neighborhood. I cannot however accurately evaluate that either. That it was followed soon by a right seventh nerve palsy is rather impressive. The statement that the facial palsy was complete indicates that it was of the peripheral type.

At this point a diagnosis of brain tumor was made and x-ray treatment given with strikingly good results. I could not make a diagnosis of brain tumor myself on the evidence at hand. We have reason to believe the seventh nerve involvement was peripheral; the fifth nerve involvement and the ocular palsy could also have been peripheral.

We are however told that under irradiation the paralysis completely disappeared. Of course this might have been in spite of, not because of, the treatment. Since the symptoms recurred later, together with some others, I believe we may consider it likely that the x-ray was responsible for the improvement. I do not know what besides a tumor of some sort could be thus improved by irradiation. Of intracranial tumors, lymphoma and hemangioma are highly sensitive to x-ray, pituitary adenoma somewhat so, and meningioma and glioma little if at all.

Since the cranial nerve involvement was in part or entirely peripheral, one thinks of a tumor of the skull rather than of the cranial cavity. Of these angiomata and xanthomata are radio-sensitive.

The story is resumed five months later with a return of symptoms—recurrence of headache, attacks of unconsciousness without aura, convulsions or incontinence, diplopia again, and the new symptoms of vomiting and bleeding from somewhere in the region of the nasopharynx. Deafness in the right ear and staggering are added to the picture. This suggests eighth nerve involvement or involvement of the ear itself.

The urine and blood pressure were normal, so that I would conclude that he did not have Bright's disease in 1917.

The physical findings of importance outside the nervous system are the bleeding granular mass in the right side of the nasopharynx and the lump on the sternum. The neurologic evidence amounts to a difference in pupils which may be sympathetic, right and also apparently left sixth nerve palsy, right fifth and seventh nerve paralysis, the latter of peripheral type. The defective hearing on the right seems to be of the middle ear type, because bone conduction is better than air. The finding of that lesion near the eustachian tube is interesting in relation to the type of deafness that was found on the right side.

The laboratory findings of importance are the anemia in the blood and the increased protein and sugar in the spinal fluid. The spinal fluid findings boil down to increase in protein, sugar and some red cells, and this colloidal gold test, which is pathologic, but what it means I am sure I do not know. He has some degree of anemia, and we know he has lost a little blood by mouth or nose but apparently not a great deal. I do not think that the finding of slight leukopenia is helpful. Neither the eyegrounds nor the lumbar puncture show evidence of increased intracranial pressure. The spinal fluid findings are consistent with brain tumor.

To hook all these phenomena together requires a fairly extensive or multiple type of lesion. There is evidence of involvement not only of the cranial cavity but also of some of the cranial nerves peripherally as well. Furthermore, the involvement is bilateral. You will recall the left sixth and later the left seventh. The lesion includes not only the cranial cavity but the nasopharynx and perhaps the ear. An extensive lesion of the skull, presumably neoplastic, is suggested. Our inclination is to link the sternal tumor with the cranial. Is one a metastasis from the other, or are both metastatic from somewhere else? The response, if it were so, to irradiation may give us a clue. It is compatible with hemangioma or xanthoma. We are told that the sternal biopsy caused profuse bleeding; this also suggests hemangioma. Fur-

thermore the fact that hemangiomata may be multiple supports such a hypothesis. The lesion in the nasopharynx can be similarly explained. At this stage multiple hemangiomata would seem a reasonable hypothesis, though I am far from being able to make such a diagnosis with confidence.

At this stage we might ask Dr. Holmes if he can help us.

DR. GEORGE W. HOLMES: In a case as complicated as this the report from the records is better than any interpretation I can give you from the films alone. When the report was written we had a better opportunity to study the film and the fluoroscopic findings.

The age of the patient may be of considerable importance,—whether or not he is of the cancer age. This patient is thirty-nine, which really does not help us at all.

The tumors which metastasize to bone with the greatest frequency usually involve the bone of the pelvis first. Carcinoma of the prostate is such a tumor. If the pelvic bones are negative we can usually rule out such a tumor. The tumors that metastasize to the brain most often are from the lung. Hypernephroma might be another tumor to be considered.

We have nothing in the chest film to suggest primary carcinoma of the lung. It can occur without the x-ray showing it, but in most cases the tumor is primary in the bronchus and there is evidence of bronchial obstruction early.

DR. MEANS: Can you say something about the sternum?

DR. HOLMES: The sternum as a rule is a very difficult bone to show by x-ray. It does not show anything here, but I am not surprised at that.

Another tumor we should think of is multiple myeloma, but this should have shown in the bones of the pelvis or the ribs. Here is the lesion we spoke of, an area of bone destruction in the parietal region. Such a shadow as that I think is definitely pathologic. There is no anatomic variation that would give such an appearance. We have definite evidence of a destructive lesion in the bones of the skull. If we rule out syphilis there is hardly anything left but malignant tumor. I do not see how any other process that involves the skull could give such an appearance.

If it were tumor primary in the brain and had destroyed the skull there should be evidence of increased intracranial pressure or increased blood supply to that region. From this film alone I would suspect that the process was of metastatic origin.

Here are the areas of calcification that were described. We interpreted these as having no definite bearing on the case. The calcification is in the region of the ligaments which run from the posterior clinoid process to the petrous portion of the temporal bone. The pineal gland is visible here and is in the normal position. A tumor in this area large enough to erode the posterior clinoid process and have calcification in it such as this should have displaced the pineal to some extent. The other calcification in the choroid plexus is of no importance.

The thinning here was described as an erosion. I rather think it is. It is outside the sella in the floor of the skull. A meningioma in that region is rare. If it were a meningioma I should expect some change in the blood supply or evidence of increased intracranial pressure.

These films were taken to show the internal auditory canals. Here is a film which shows the shadow which we saw in the lateral view. It is interesting because it might easily be mistaken for something within the eyeball. I do not believe it has much to do with the problem. These films were taken to show the petrous tips; they do not give us any help.

DR. MEANS: By x-ray there seem to be changes in the sella turcica, not of the sort seen in pituitary disease, which enlarges it by pressure from within, but rather as from a lesion encroaching from without, in the middle fossa of the skull. I rather expected that some evidence of involvement of the petrous portion of the temporal bone would be found, but such is not the case. The lesion of the occipital bone is interesting because it does indicate a tumor, but I cannot relate it to the symptoms.

With all these facts in mind I incline to a diagnosis of a multiple neoplastic lesion involving the regions I have mentioned. Metastatic malignant disease should show more bony change. Lymphoblastoma should show evidence elsewhere in the body. Dr. Holmes has mentioned multiple myeloma. This tumor seems to me to have extended too far beyond the actual bony tissue to be consistent with myeloma. Hemangioma therefore I believe most nearly fills the bill. I am impressed with the profuse bleeding from the biopsy. Then too there were those red cells in the spinal fluid.

FURTHER HISTORY

Three days after operation he developed a complete paralysis of the left upper facial. His temperature dropped from 105.4° to 99°. On the following day the temperature rose to 105.7° and continued elevated until his death on the eleventh day after admission.

FURTHER DISCUSSION

DR. MEANS: Why a sternal biopsy should lead to his death I cannot imagine. Yet apparently it did. There was hemorrhage, but this does not explain the rapidly climbing temperature. Except for one drop to normal on the eighth day, he had a steadily climbing temperature reaching a level of 105°, a steadily rising pulse, and finally a climbing respiratory rate. I cannot square the picture with actual infection at the time of operation. I rather suspect that

something happened at the time in his head, hemorrhage from the vascular tumor perhaps, with fever due to disturbance in the temperature regulating center. I am reminded of a similar type of thermal response in a man who had been poisoned by several drugs, of which cocain was one. It was thought then that his fever was due to a paralysis of the heat center.

Clinical Discussion

Dr. Tracy B. Mallory: The biopsy from this patient's sternum five days before his death showed a typical plasma cell myeloma. Subsequent to the receipt of that diagnosis the urine was reëxamined for Bence-Jones proteins by Dr. Jacobson and they were found. At previous examinations of the urine before the diagnosis was known it had been reported as negative or as showing only a trace of albumin, as given in the summary.

Dr. Mixter, you had a chance to see this patient. Have you anything to say?

Dr. W. Jason Mixter: I have not very much to add to Dr. Means' discussion of this case. I have definite recollections of the patient on account of the fact that he was so evidently a seriously sick man when he came to the hospital. His general condition was precarious, more so than is demonstrated in his chart or his physical examination. The impression that one got of the man was that he was a very sick patient who would take very little to knock him out, and I think that is proved by the fact that he died promptly following the biopsy, which was not much of an operation. Although there was a good deal of bleeding, it was not extensive, not of a character to have caused his death, and was promptly controlled by packing the wound.

The whole case was a distinctly puzzling one on account of the length of time that the cranial symptoms had been going on. There was very little pointing to lesions elsewhere. The finding of a tumor in the sternum when the patient arrived here and the finding of a punched-out hole in the skull by x-ray both spoke for a malignant process. Those had not been observed when he had been previously studied in another city. The case seemed to us to be clearly one of a multiple malignant lesion of unknown pathology which we attempted to demonstrate with this result.

Dr. James B. Ayer: I have nothing to add except that it is very unusual I should say, as Dr. Holmes has intimated, that multiple myelomas should not appear elsewhere. Practically all of our cases do show numerous bone lesions other than those that were demonstrated here.

Dr. Mallory: Have you anything to add, Dr. Cabot?

Dr. Richard C. Cabot: Only one small point about this man. He was not my patient, but I stayed a week at his house six months before his death. No one would have thought, knowing him as a friend, that he would die within six months. He had a squint in one eye and when he read he would put his hand over this eye. I was with him all the time. I simply want to testify that a man with this illness can be as well as I saw him six months before his death.

Dr. Tracy J. Putnam: One thing that strikes me about the spinal fluid findings is this extraordinary gold curve. I think that is enough to rule out a single very large tumor, and on the other hand I think it is enough perhaps to rule in some kind of abnormal tumor, probably not infectious, within the cranial cavity.

It is possible that the reason the pressure was not higher was that the patient was vomiting and partially dehydrated himself in that way.

I am interested in the high temperature and the rapid decline of the patient following biopsy and should be inclined to consider that also as evidence of multiple neoplastic lesions, which often produce severe and fatal symptoms, often a terminal hyperthermia, without a high intracranial pressure.

Dr. Mallory: Dr. Jacobson, would you like to say a word?

Dr. Bernard M. Jacobson: After we were told of the result of the biopsy the natural thing to do was to test the urine for Bence-Jones protein. It was easy enough to find it then. At the same time the urine that I tested contained a good trace of albumin by nitric acid test. It is a very rare finding not to observe a large amount of albumin in these patients at practically all times, and I should be inclined, looking back, to doubt the validity of the very slight trace of albumin at the first examination.

Dr. Mallory: Over a six or seven year period I think there were only two out of twelve or more cases of multiple myeloma in which Bence-Jones protein was found in the routine examination. This last year Dr. Jacobson has found it I think in every case he has examined for it.

Dr. Jacobson: I have examined four cases and they have all shown it.

A Physician: Were blood smears done in this case?

Dr. Mallory: Only one, and no abnormal cells were noted.

Dr. Holmes: There is one point in the interpretation of that lateral view of the skull which I should have mentioned and which would have helped Dr. Means a little. In hemangioma the blood vessel channels surrounding the lesion should be enlarged. There is no enlargement here.

Dr. Means: I should like to ask Dr. Holmes if hemangioma does get into the bone and produce an area of decreased density under any circumstances, or whether that was an absolutely

impossible thing to suggest. I should also like to ask him if myeloma responds to irradiation in the way this tumor apparently did at the first admission.

DR. HOLMES: In answer to the first question, I think it does, but there is always an accompanying enlargement of the blood vessels, a different picture from that of the ordinary metastatic tumor and different from this case.

The response of hemangioma to irradiation is not so prompt as a rule as this was, although they do respond very well. The response of myeloma to radiation varies tremendously. Some of the cases do respond as this one did. I think that is more apt to be true of the plasma cell type. Other forms of myeloma, particularly of the slowly growing type, show very little response. It would be interesting to know how large a dose the patient was given. In most of the cases where we are uncertain as to diagnosis we give a dose below the erythema, and in that case I should not have expected much to happen to myeloma.

CLINICAL DIAGNOSES (FOLLOWING BIOPSY)

Multiple myeloma.

ANATOMIC DIAGNOSES

Multiple plasma cell myeloma involving the sternum, the brain, the skull and the right kidney.
Lobar pneumonia, bilateral.
Acute fibrinous pleuritis with effusion, bilateral.
Hyperinvolution of the thyroid.
Operation wound, sternal biopsy.

PATHOLOGIC DISCUSSION

DR. MALLORY: The autopsy on this man showed multiple lesions of the skull which had eroded the inner table and had partially invaded the meninges and the pia, but had not actually gone into the brain at any point. The lesions were so placed that the fifth nerve was completely destroyed by tumor. The third and sixth nerves were not involved within the cranial cavity, but were involved where they went through the cavernous sinus.

A nodular mass one centimeter and a half in diameter protruded through the right internal acoustic meatus and so involved the seventh and eighth nerves on that side. The ninth, tenth, eleventh and twelfth nerves were uninvolved.

In the body as a whole we found a terminal lobar pneumonia which apparently had been entirely unsuspected clinically. The liver showed a small tumor 1.5 centimeters in diameter which was very vascular and red. We thought without question from the gross that it was one of the common congenital hemangiomas of the liver, but it turned out to be a tumor composed entirely of myeloma cells, in other words a metastasis. The tumor of the pharynx seems also to be myelomatous.

One point not generally recognized, though we have seen a number of cases, is the frequent involvement of the pharynx in multiple myeloma. Parker, Jackson and Bethee* at the City Hospital have reported four cases in which a primary diagnosis of plasmocytoma was made from a biopsy of the tonsil or of cervical lymph nodes two, three or even seven years before the typical changes of myeloma appeared in the bones. There is at the present time a patient in the Eye and Ear Infirmary with a tumor of the nasopharynx that was biopsied, showed plasmocytoma, and that case also has subsequently been x-rayed and proved to have multiple myeloma.

A PHYSICIAN: Do they usually bleed?

DR. MALLORY: The tumors in this case are exceptionally vascular.

Gross examination of the other bones of the body was entirely negative except for the sternum. Microscopically scattered throughout the marrow are miliary areas of myeloma averaging one half to one millimeter in diameter. None of them is greater than that, so that they were distinctly too small to be seen by x-ray.

A PHYSICIAN: Were the kidneys negative?

DR. MALLORY: The kidneys were practically negative. There was slight arteriosclerotic nephritis, not the so-called myeloma kidney, with an enormous number of casts.

*Jackson, Henry, Jr., Parker, Frederick. Jr., and Bethee, James M., Am. J. Med. Sci. 181:109, 1931.

CASE 20032

PRESENTATION OF CASE

A thirty-two year old Canadian Duco sprayer entered complaining of loss of vision and failure of the eyes to move.

Seven days before admission the patient noticed a blurring of vision, as if there were a mist before his eyes. He had had some rather indefinite difficulty with his vision during the past year for which he had worn glasses. His present attack was different in character, and increased in severity for two days, when he began to have spells of stupor from which he was aroused with difficulty. He also complained of some headache, but this was not a prominent symptom. His periods of stupor became more severe during the next few days and at times his speech was rather incoördinate. He was observed at this time to tend to fall to the left, and often his face was drawn to one side. The side of the face involved was not definitely determined. It was later found out that he had been coughing for the past three years, bringing up a large amount of phlegm. There was also a history of his having two hemorrhages.

For the past two years and especially of late

the patient had been drinking heavily of "moonshine" and other powerful alcoholic concoctions. Recently he had been almost constantly drunk. He denied venereal disease by name and symptom.

Examination showed a well developed and well nourished man of thirty-two lying flaccid in bed in a stuporous condition from which it was difficult to arouse him. When he was aroused his answers were dull and unenthusiastic. His memory appeared very uncertain. The eyegrounds were very difficult to see. The right disk appeared fairly normal. He was able to see fingers at six feet. The right eye did not move at all; the left moved very slightly. Both pupils were fixed. The left was slightly larger than the right. Both eyelids showed ptosis. Light touch over the face was equal on both sides, but pin prick could be felt better on the right than on the left. The corneals were both present. The jaw was in the midline. There was no facial weakness. Both eyes closed. There was no abnormality in the function of the eighth, ninth, tenth, eleventh and twelfth cranial nerves. The left arm was weak in all movements. The legs seemed equal in strength. Both the left arm and the left leg appeared more flaccid on passive movement. There was no atrophy or fibrillation. The reflexes were all normal except for a left positive Babinski. Position sense was normal. There was a fairly good finger-to-nose test. The other cerebellar tests could not be done.

The findings on examination of the blood were within normal limits. The Hinton and Wassermann tests were negative. A lumbar puncture showed an initial pressure of 225 with normal oscillations. The spinal fluid showed eight lymphocytes. Alcohol test was positive. Ammonium sulphate test was negative. The total protein was 80. The Wassermann was negative.

The patient rapidly failed and died two days after admission.

Clinical Discussion

Dr. James B. Ayer: The outstanding neurological features of this case are two:—first an abnormal mental condition, essentially a stupor with memory defect, and second almost total ophthalmoplegia, both external and internal, associated with impairment of vision.

While the evidence given is somewhat conflicting, some weakness of the left arm and leg is indicated, and this palsy is of the flaccid type and yet associated with a positive Babinski suggesting pyramidal tract involvement. Sensory disturbances, except for a doubtful hypesthesia of the left face, are conspicuous by their absence, both in the history and on examination, and we see no note as to muscular arhythmias, convulsions, ataxia or asynergia.

The sole localizing sign appears to be total ophthalmoplegia, and this is such a conspicuous sign that I think we are entitled to analyze the case with this as a basis. So far as I know lesions causing fixation of both eyeballs with dilated and fixed pupils have uniformly been found in or about the midbrain and corpora quadrigemina. Such lesions have been tumors, tuberculoma, syphilis, hemorrhage and certain toxic or infectious states to which the name of polioencephalitis superior has been given.

In this case tumor seems unlikely because of the apparent rapidity of course without evidence of increased intracranial pressure (absence of choked disks and only slight elevation of spinal fluid pressure). Tuberculoma also seems unlikely for the same reasons, but a productive cough for three years and two hemorrhages (perhaps from lung) together with a few lymphocytes in the fluid make this diagnosis a possibility, although it is not clear why his vision had failed or why he was in a stupor—obviously not from tuberculous meningitis.

Polioencephalitis superior acute hemorrhagica of Wernicke is described in textbooks as petechial hemorrhages in the midbrain causing total ophthalmoplegia, and is said to occur in alcoholics. Recovery is said to be frequent. I see no reason why hemorrhage limited to this site should cause death, and there is no indication that gross hemorrhage into the ventricles or meninges did occur, either spontaneously or on a traumatic basis. Mesencephalic syphilis is common, and while subtotal ophthalmoplegia of one eye is not rare, I do not recall a single case in which both eyes were involved. In mesencephalic neurosyphilis the serology is uniformly positive.

Although I have not seen it I here favor the diagnosis "toxic polioencephalitis" which has been described in alcoholic intoxication (methyl, I believe), carbon monoxide poisoning and botulism. In all of these conditions, besides the oculomotor paralysis mental abnormalities and visual disturbances of the type here given have been described, and at times paralysis of limbs also. In all the onset and course have been said to be rapid, leading frequently to death. In such conditions microscopic lesions have alone been found, if any.

Still one more disease should be mentioned in this connection, i.e., chronic progressive ophthalmoplegia, an example of which I saw only last week. The long course over many years and the absence of associated symptoms render the diagnosis untenable in this case.

Clinical Diagnoses

Meningovascular lues?

Anatomic Diagnoses

Glioma, unclassified, of midbrain.
Congestion and edema of the lungs.

Chronic fibrous pleuritis, bilateral.
Kyphoscoliosis.

Pathologic Discussion

Dr. Charles S. Kubik: Section through the midbrain reveals a tumor which is about two centimeters in diameter. The greater part of it is in the tegmental portion and on the right side, but it extends far enough to the left to destroy almost all of the quadrigeminal plate and to involve both third nerve and fourth nerve nuclei. It occupies the site of the right medial lemniscus and touches but apparently does not invade the right cerebral peduncle. Although the aqueduct is completely flattened out, the lateral ventricles are enlarged very little if at all.

Most of the clinical localizing signs are explained very nicely by the findings. Since the third nerve supplies the constrictor of the pupil and all of the external ocular muscles except the superior oblique, which is supplied by the fourth nerve, and the external rectus, supplied by the sixth nerve, the explanation of the ophthalmoplegia, excluding paralysis of external recti, is obvious. Since the tumor does not extend to the fourth nerve nuclei the reason for paralysis of the external recti is not so clear but is probably to be found in involvement of the posterior longitudinal bundle. With function of the third nerve nuclei destroyed one would expect both light and accommodation reflexes to be absent, and it is not necessary to bring in the supranuclear pathway of the light reflex, although it also would unquestionably be affected.

There is involvement of the sinothalamic fibers of the medial lemniscus to account for the hyperesthesia of the left, or contralateral, side of the face, but one would have expected hyperesthesia of the entire left side. It is perhaps possible that this was present and could not be elicited because of the patient's mental condition.

For the signs of disease of the corticospinal tract we have the tumor in close proximity to the right cerebral peduncle.

Our findings do not make it clear why memory defect and stupor should have been such prominent symptoms, nor is it easy to understand why intracranial pressure was no greater with the aqueduct compressed as it is. Finally, we have not shown exactly what was the cause of death. It is possible that microscopic sections would reveal pathology which is not apparent on gross examination.

Histologically the tumor is a poorly differentiated glioma, not yet classified.

Dr. Tracy B. Mallory: The remainder of the necropsy findings cast no further light upon the case. The lungs showed the usual extensive edema and congestion found in cases of cerebral death, with very slight foci of hypostatic pneumonia, too insignificant to be of clinical importance.

The rapidity of development of the patient's symptoms and the absence of signs of increased intracranial pressure naturally led Dr. Ayer away from the diagnosis of tumor, though his localization of the process was entirely correct.

As is so often the case, the exact mechanism of death eludes us in spite of careful anatomic examination. It must always be remembered that death after all is a physiologic process which need not have its exact anatomic counterpart. In the so-called "anesthetic death" for instance, completely negative autopsy findings are the rule.

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EXAMINATIONS, EXAMINEES AND OTHERS

IT may be that the Massachusetts Board of Registration in Medicine will or will not choose to notice formally the misrepresentations and misinterpretations of its report which have appeared in the press in several parts of the state recently, but it will not be trespassing on the province of the Board to comment on the examinational procedure of state boards and the reaction thereto by certain groups of interested persons.

These procedures have been widely and intensively studied by persons who make a business of preparing candidates for the examination. Although copies of the questions are given only to candidates and each copy must be returned with the answers, the making of an additional copy during the examination presents little difficulty and complete files are in the hands of some coaches. This business of coaching is becoming less profitable. The formal "review courses" which were at one time given in the fourth year in a number of schools, have largely if not entirely disappeared.

Now the graduates of the approved schools need less and less such "review courses" in such schools and the extra mural coaching, and the graduates of the non-approved schools, in considerable proportion, cannot stand the intensive discipline which such coaching demands: they have not even that much intellectual background. It is not merely that they do not know medicine, but some of the graduates cannot be taught, even by repeating the coaching course several times. Of course some individuals can profit by it and do so, but the field for the coach is greatly restricted as now only Massachusetts accepts for examination the graduates of the non-approved schools.

The psychology of the examining board is also studied, the kind of question each examiner is likely to give, as shown by what he has given. Furthermore, it is thought that weak candidates are likely to receive less favorable consideration if they are in direct competition and contrast with the best candidates, and if the group to be examined is unusually large the examiners may prove to be more ruthless.

Therefore it may be thought to be an advantage to the weaker candidate if he does not appear at the July examination in Massachusetts which most of the candidates from the approved schools, recently graduating in June, take and pass the first time. The weaker candidates may tend to avoid the July examination and appear in November and March. The last examination, in March, and the May 1933 examination corresponded to the usual March examination, is likely to have the weakest candidates in greatest numbers.

Perhaps something of this sort actually happened in May 1933, because according to the figures, published in the *Journal of the American Medical Association*, November 25, 1933, page 1749, there were thirty-three graduates of approved schools who took the examination referred to, and sixty-five others. These figures may not be exact, as some of the National Board diplomates may have been registered in May.

It is interesting to compare the figures for the Massachusetts examination with those for the Missouri examination noted on the same page of the *Journal*. Two hundred and one candidates took the examination and all passed; also, all were from approved schools as no others are eligible in Missouri. The graduates of non-approved schools are admitted to examination in no state besides Massachusetts. Why does the law admit them to examination here? "There's a reason."

Another device by which, perhaps unknown to the candidates themselves, they may be directed to the so-called more favorable examination, is the requirement of an interne year be-

fore the degree is conferred. There is some irregularity in dates of termination of the internships and thus a tendency to throw the date of receiving the degree beyond the examination least favorable for the weaker candidates.

The Annual Report of the Board shows no study of the returns from the points of view which have been suggested, but it might be illuminating if the Board should think it worth while to consider this aspect of the question in some future report.

THE TUBERCULOSIS MORTALITY RATE

THE latest publication in *The Spectator* relating to pulmonary tuberculosis mortality by Dr. F. L. Hoffman, shows that, although there is a wide range in the deathrate of this disease in different localities, the real trend is toward lower figures in fifty-nine cities of the United States having a combined population in 1932 of 33,044,067.

In 1931, the figures for this group were 63.2 per 100,000 whereas in 1932, they were 56.3. In 1910 the record is 174.4 for the same cities. The reduction is practically coincident with the life of the National Tuberculosis Association, and is due in large measure, according to Hoffman, to the public health policies of the several states. Fortunately a concerted attack on this disease prevails throughout the civilized countries of the world.

Although this result "challenges the admiration of mankind", there is an annual loss in this country from pulmonary tuberculosis alone of 75,000 persons, and the problem now before the people is how to reach the irreducible minimum.

Looking at the problem in a general way, there seems to be one stumbling block in the pathway of reduced mortality from this disease in the Negro race where the rate is especially high, and this calls for an awakened community spirit in those localities where concentration of colored people exists.

Dr. Hoffman uses the urban rate of 48.1 of New York State exclusive of that of New York City, as compared with the rural rate of 72.7, to call for an adequate explanation which may be of exceptional interest because of the usual belief that rural areas are more healthful than cities. He suggests that the "assumption that the country is more favorable for the prevention and treatment of tuberculosis than large cities", although not statistically supported, may be explained by the increased deathrate in the country areas in New York State, due to the tuberculosis sanatoria located in rural sections.

These figures and suggestions show that the tuberculosis problem presents opportunities for extended and concentrated studies if further advances are to be made, for it is generally accepted that this disease constitutes the greatest menace to life in the ages between eighteen and forty.

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

CLUTE, HOWARD M. B.S., M.D. Dartmouth Medical School 1914. F.A.C.S. Surgeon, Lahey Clinic. Visiting Surgeon, New England Baptist Hospital and New England Deaconess Hospital. Address: 605 Commonwealth Avenue, Boston. Associated with him is

PILCHER, LEWIS S. II. B.A., M.D. Harvard University Medical School 1930. Fellow in Surgery, Lahey Clinic. Address: 605 Commonwealth Avenue, Boston. Their subject is "The Place of Iodine in the Treatment of Goiter." Page 117.

JONES, T. DUCKETT. B.A., M.D. University of Virginia Medical School 1923. Research Director, House of the Good Samaritan. Assistant in Medicine, Massachusetts General Hospital. Instructor in Medicine, Harvard Medical School. Address: 25 Binney Street, Boston. Associated with him is

MOTE, JOHN R. A.B., Student, Harvard Medical School Class of 1935. Address: 107 Avenue Louis Pasteur, Boston. Their subject is "The Phases of Foreign Protein Sensitization in Human Beings." Page 120.

HEALY, JAMES C. Ph.G., M.D. Tufts College Medical School 1927. Junior Visiting Physician, Boston City Hospital. Assistant Visiting Physician, Long Island Hospital, Boston. Instructor in Medicine, Tufts College Medical School. Address: 520 Commonwealth Avenue, Boston. Associated with him is

GALLISON, DAVIS T. Ph.B., M.D. Tufts College Medical School 1924. Junior Visiting Physician, Boston City Hospital. Instructor in Medicine, Tufts College Medical School. Address: 520 Commonwealth Avenue, Boston. And

BRUDNO, JAMES. A.B., M.D. Tufts College Medical School 1931. Formerly House Physician Third Medical Service, Boston City Hospital. Assistant in Medicine, Tufts College Medical School. District Physician, Boston Dispensary. Address: 170 Holbrook Road, Quincy. Their subject is "Gastro-Intestinal Allergy Associated with Transient Intraventricular Block." Page 123.

ROOT, HOWARD F. See page 44, issue of January 4, for record of author. His subject is "The Association of Diabetes and Tuberculosis. III. Clinical Features." Page 127.

NISSEN, H. ARCHIBALD and SPENCER, K. A. See page 44, issue of January 4, for record of authors. Their subject is "Arthritis and Systemic Involvement as Exemplified in A Group of Dead Arthritics." Page 147.

STEWART, COLIN C., JR. A.B., M.S., M.D. University of Pennsylvania Medical School 1926. Member of the Staff of the Mary Hitchcock Memorial Hospital, Hanover, N. H. His subject is "Neurofibromatosis in Children: Report of Two Cases." Page 150. Address: Hanover, N. H.

MISCELLANY

TESTIMONIAL DINNER TO DR. G. F. MARTIN

The associates of Dr. G. Forrest Martin on the staff of the Lowell General Hospital tendered a testimonial dinner to him on December 7, 1933, on the occasion of his retirement as senior surgeon after forty years of active service. Several speakers, including toastmaster Dr. C. Stoyle Baker; John F. Sawyer, chairman of the executive committee of the hospital; Dr. Archibald C. Gardner, Dr. Martin's successor as senior surgeon; Dr. Howard Jewett, a friend and associate of the guest of honor, and Dr. John Nichols, superintendent of the Tewksbury Infirmary, of which Dr. Martin is a trustee, praised Dr. Martin's years of outstanding service to the hospital and to the community.

Dr. Martin, in replying, recalled the early days at the hospital, contrasting the methods employed during the '90's with those of modern times. He concluded with a tribute to the hospital itself and a plea to the younger doctors to give it their unqualified support. Dr. Martin will continue as a member of the board of trustees and as a consultant.

EMERGENCY CAMPAIGN

At a recent meeting in the Boston Medical Library, plans were perfected for a canvass of the physicians of Greater Boston in the interests of the Boston emergency campaign. In this organization a committee of two hundred and twenty physicians will serve under the chairmanship of Dr. Channing Frothingham. Subscription blanks, Dr. Frothingham announced, will be provided for every physician practicing in the area served by the drive, as well as for the physicians' employees.

RADIO TALKS ON SPEECH CORRECTION

To further the campaign of the American Society for the Study of Disorders of Speech to extend speech correction in the public school system of the United States, a series of radio talks will be given by Samuel D. Robbins, Secretary of the Society. These talks are to be delivered at 2:45 on Sunday afternoons over WLEY (1370 kilocycles). The program follows:

January 21. What Causes Speech Defects.

January 28. How Parents and Teachers Can Correct Baby-Talk.

February 4. One-act Play, "Nicked."

February 11. How to Prevent Stammering from Becoming Confirmed.

February 18. Use of Suggestion and Distraction in Correcting Stammering.

February 25. Use of Rhythm in the Correction of Stammering.

March 4. One-act Play, "A Peculiar Old Duffer."

March 11. How Calm Breathing Reduces Stammering.

March 18. How to Overcome Feeling of Insecurity.

March 25. How Stammerers Can Overcome Neurotic Traits.

April 1. Thirty Earmarks of the Normal Adult.

April 8. Request Night. Mr. Robbins will answer questions.

WILLIAM LAMBERT RICHARDSON PROFESSORSHIP OF PEDIATRICS

The creation of a new endowed professorship at the Harvard Medical School has been announced by the University. The new chair has been established under the will of the late William Lambert Richardson, former Professor of Obstetrics and Dean of the Harvard Medical School, who died in October, 1932. In his memory, the Harvard Corporation has voted to name the chair the William Lambert Richardson Professorship of Obstetrics. The first incumbent will be named at the next meeting of the Harvard Board of Overseers on February 26.

Dr. Richardson graduated from Harvard College in 1864, and from the Harvard Medical School in 1867. For 36 years from 1871 to 1907 he served as a member of the teaching staff at the Medical School, acting as Dean from 1893 to 1907. From 1909 to 1915 he was a member of the Board of Overseers.

In his will, Dr. Richardson gave $100,000 to the President and Fellows of Harvard College to endow a Professorship of Obstetrics. He also gave $40,000 to establish the Jeffrey Richardson Fellowship in the Harvard Medical School, the income to be awarded each year by the Faculty of Medicine to some deserving student of the Medical School who wishes to continue his studies after graduation.

DR. CUTLER NAMED HARVARD MARSHAL

Dr. Elliott C. Cutler, professor of surgery at the Harvard Medical School and surgeon-in-chief of the Peter Bent Brigham Hospital, has been elected by the directors of the Harvard Alumni Association as chief marshal of the Commencement exercises of the Alumni Association next June.

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR DECEMBER, 1933

Lobar pneumonia shows a high incidence for the month. In December, 1925, there were 715 cases and in December, 1918, 1203 cases.

Whooping cough and measles continue to be reported in numbers considerably above last year and the preceding five year average.

Amebic dysentery, with Chicago origin, has been reported 17 times to date with no secondary cases.

Diphtheria, typhoid fever, and pulmonary tuberculosis reached their lowest December incidence.

Tuberculosis, other forms, anterior poliomyelitis, mumps, scarlet fever, and chicken pox show nothing remarkable.

RARE DISEASES

Anterior poliomyelitis was reported from Dudley, 1; Fall River, 1; Longmeadow, 1; Weymouth, 1; total, 4.

Anthrax was reported from Peabody, 2.

Amebic dysentery was reported from Belchertown, 1; Boston, 2; Brookline, 1; Canton, 3; Winchester, 1; Worcester, 1; total, 9.

Encephalitis lethargica was reported from Everett, 1.

Epidemic cerebrospinal meningitis was reported from Cambridge, 2; Haverhill, 1; North Adams, 1; total, 4.

Malaria was reported from Chelsea, 1; Worcester, 1; total, 2.

Septic sore throat was reported from Boston, 4; Cambridge, 1; Clinton, 1; Grafton, 1; Lowell, 1; Northampton, 1; Palmer, 1; Somerville, 1; Wakefield, 2; Westboro, 1; total, 14.

Tetanus was reported from Attleboro, 1.

Trachoma was reported from Worcester, 2.

Trichinosis was reported from Beverly, 1.

Typhus fever was reported from Boston, 1.

Undulant fever was reported from Holden, 1.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

MONTHLY REPORT FOR DECEMBER, 1933

Disease	Dec. 1933	Dec. 1932	Average*
Anterior Poliomyelitis	4	3	14
Chicken Pox	1028	1700	1489
Diphtheria	99	156	353
Dog Bite	300	318	287
Epidemic Cerebrospinal Meningitis	4	6	9
German Measles	30	28	59
Gonorrhea	593	613	509
Lobar Pneumonia	740	374	415
Measles	2251	519	1293
Mumps	367	527	481
Scarlet Fever	843	1527	1252
Syphilis	372	369	321
Tuberculosis, Pulmonary	255	305	324
Tuberculosis, Other Forms	29	25	40
Typhoid Fever	15	17	23
Undulant Fever	1	1	—
Whooping Cough	1144	669	687

*Average number of cases for December during the preceding five years.

RESULTS OF SYRACUSE HEALTH PROGRAM RECORDED IN "A CITY SET ON A HILL"

HISTORY OF SYRACUSE HEALTH DEMONSTRATION TOLD BY DR. C.-E. A. WINSLOW

Doubleday, Doran & Co., Garden City, New York

Coming at a time when the nation-wide cry is that appropriations for all varieties of public services be cut to the smallest amounts possible in order that budgets may be balanced, the publication today of a book which shows in dollars and cents the value of an adequate city health organization becomes a matter of importance to everyone concerned with public affairs. The book is "A City Set on a Hill," in which Dr. C.-E. A. Winslow discusses the significance of the health demonstration at Syracuse, New York, conducted by the Health Department of that city in coöperation with the Milbank Memorial Fund, and is issued by Doubleday, Doran & Co. Dr. Winslow is professor of Public Health at the Yale School of Medicine and since 1929 has been a member of the board of scientific directors of the Rockefeller Institute and expert assessor of the Health Committee of the League of Nations.

The Syracuse demonstration was carried on for the ten years preceding 1932 in an effort to determine whether an adequate investment in health by a city would produce a perceptible effect on public welfare and whether it would yield returns in decreasing death and disease figures. During this period per capita health appropriations were increased from $1.00 to $2.08 per year. The scope of the activities included among other things water supply, waste disposal, communicable disease, tuberculosis, venereal disease, health problems of maternity and infancy, school health, public health nursing, cancer, heart disease, mental hygiene and industrial safety.

The report shows "that public health work pays dividends," in that with a health program in 1931 costing $500,000, Syracuse effected an annual economic saving in only three groups of disease of well over $2,000,000.

At the time the demonstration was inaugurated in Syracuse many excellent movements had been inaugurated and some carried to completion, but the health program of the city as a whole was uncoördinated and, particularly in the nursing field, inadequate.

Dr. Winslow says that "the three most immediate needs of the Syracuse health program lay in the fields of communicable disease, tuberculosis, and health education. These three problems were therefore carefully studied by the Health Department and other local agencies with the coöperation

of the State Department of Health and the State Charities Aid Association; and definite programs were developed along all three lines. A full-time assistant to the health commissioner was temporarily lent to the city by the State Department of Health. In the first year of the demonstration (1923), the Bureau of Communicable Disease was reorganized with a part-time director and a full-time medical assistant, two nurses were employed for communicable disease service, and an active campaign for diphtheria immunization was launched.

"The demonstration has been completely successful in its first major task of convincing the community as a whole of the value and importance of an adequate public health program."

According to the author, outstanding items of progress are as follows: reorganization of the Department of Health under a full-time commissioner, with eleven bureaus of which all but three have full-time heads; the establishment of a sound system of vital statistics and record-keeping; the development of a program for the control of tuberculosis which Sir Arthur Newsholme pronounced "the best I have known in any area in America"; the coördination of the work of various agencies working in the field of maternal and infant hygiene into a compact program of excellence; the coördination of the health program for children in public and parochial schools under a single director; the combination of specialized nursing services into a well-organized and well-supervised staff for generalized public health nursing; an excellent and effective campaign for immunizing school children and preschool children against diphtheria; a well-planned program of popular health instruction; a demonstration program of visiting teacher service, and the organization of a health council and of a strong citizens' committee for the support of the community health program.

All of these activities are discussed and it is emphasized that the citizen must ask himself whether the cost of being governed, with its protection of life and property, the safeguarding of health and the education of children, is worth the cost.

"We have seen," he says, "that even an unusually complete and adequate community health program, such as Syracuse enjoyed in 1931, costs about two dollars per capita per year. Two dollars would buy a dozen gallons of gasoline, a theatre ticket, a carton of cigarettes, or a box of candy. The particular two dollars spent on the average by each citizen for health bought a clean and sanitary city; protection against epidemics of smallpox, typhoid fever, and diphtheria; the saving of the lives of hundreds of infants; the reduction of tuberculosis, once the greatest scourge of mankind, to a minor rôle in the death rate."

CORRESPONDENCE

SYPHILIS IN PARIS IN EARLY DAYS

Mr. Editor:

The following account is from F. Campbell Stewart's interesting book, "Eminent French Surgeons and Hospitals of Paris," published in this country in 1843. The quotation comes from the article on the "Hôpital du Midi."

This hospital was originally a convent built by the Capucin Friars and occupied by them until 1784. Stewart tells us that it was "then erected into a hospital for nurses and new-born children afflicted with Syphilis. In 1792 adult patients of both sexes were introduced, and it became a general venereal hospital."

Stewart continues: "Syphilis is said to have made its appearance in France during the reign of King Charles VIII, when it created such consternation and alarm, that all who were affected with it were sent to Salpêtrière and Bicêtre, where they were placed, the sexes together, four or five in a bed, and never allowed to leave the apartment in which they were confined, during the whole course of their treatment, which was usually of a year's duration." . . . "Such as came from the country to be cured at Paris were immediately sent back, and prohibited from returning to the city under *pain of death.*

"Those who were affected with the disease in Paris were *publicly whipped* at the beginning of their treatment; and also at its termination.

"The consequence of these severe and unwise regulations was to induce those suffering with the disease to conceal it as long as possible from the authorities; hence, when detected, it was found always to exist in an aggravated form.

"The condition of the poor sufferers from syphilis was ameliorated under the reign of Louis XVI; but it is only since the first Revolution that the necessary care has been bestowed upon them."

Very truly yours,

WM. PEARCE COUES, M.D.

January 11, 1934

THE CAUSE OF DRYDEN'S DEATH AND HIS FUNERAL

Mr. Editor:

The following is from Samuel Johnson's "Lives of the Most Eminent English Poets":

"The time was now at hand which was to put an end to all his schemes and labors. On the first of May, 1700, having been some time, as he tells us a cripple in his limbs he died in Gerard Street of a mortification in his leg."

Johnson gives this account of Dryden's funeral ("By a writer I know not what credit"). He tells us that a roistering nobleman, Lord Jeffries, and his crew, came upon the funeral cortege and insisted on a public funeral in the Abbey. Lady

Elizabeth Dryden was not willing for this and said, "No, no."

Lord Jeffries' crew stated that Lady Elizabeth had said, "Go, go," and arrangements were made at the Abbey, the choir in attendance, and an anthem set.

After three days of waiting the undertaker saw Lord Jeffries, who said he knew nothing whatsoever of the matter.

"In this distress Dr. Garth sent for the corpse to the College of Physicians, and proposed a funeral by subscription to which himself set a most noble example. . . . Dr. Garth pronounced a fine Latin oration at the College over the corpse."

Johnson speaks of Edward Ward's account of these occurrences in his "London Spy," 1706, and states that according to Ward, "The cause of Dryden's death was an inflammation in his toe, occasioned by the flesh growing over the nail, which being neglected, produced a mortification in his leg."

"In the Register of the College of Physicians is the following entry: 'May 3, 1700. Comitiis Censoriis Ordinariis. At the request of several persons of quality that Mr. Dryden might be carried from the College of Physicians, to be interred at Westminster, it was unanimously granted, by the President and Censors.'"

Johnson remarks that this entry "Is not calculated to afford any credit to the narrative concerning Lord Jeffries."

From the statement of Dryden that he was for some time a "Cripple in his limbs," and the account of Edward Ward in the "London Spy," it seems likely that Dryden suffered from arteriosclerosis of his leg vessels, an ingrowing toe nail, and subsequent infection, resulting in arteriosclerotic gangrene of the leg.

Very truly yours,

WM. PEARCE COUES, M.D.

January 5, 1934

GOLD MINERS' CURE FOR THE SCURVY

Editor, *New England Journal of Medicine*,

The following account is from "A Quaker Forty-Niner, the Adventures of Charles Edward Pancoast on the American Frontier."

Philadelphia, University of Pennsylvania Press, 1930.

"During the time we were operating here I became afflicted with scurvy, and sores of a very vicious character broke out all over me. The long continued use of salt meat without vegetables caused many miners to become so afflicted, and the only remedy known to us was to bury the patients in the earth with their faces uncovered, and allow them to remain in that position from seven to nine days. I did not fancy this remedy, so I went to the Trading Post above us to consult with our Dr. Rogers who had located there. He gave me a box of quinine pills and directed me to procure potatoes, slice them up in vinegar, and eat them plentifully as a salad three times a day, at the same time abstaining from salt meat. In consideration of my membership in his Company, he charged me only $50.00, with two boxes of Quinine Pills thrown in, but this was cheaper than being buried. I procured potatoes at a dollar a pound, following the Doctor's directions, and in six weeks was cured."

Yours truly,

WM. PEARCE COUES, M.D.

January 3, 1934

ARTICLES ACCEPTED BY THE AMERICAN MEDICAL ASSOCIATION COUNCIL ON PHARMACY AND CHEMISTRY

535 North Dearborn Street,
Chicago, Illinois,
January 4, 1934.

Managing Editor,
The *New England Journal of Medicine*,

In addition to the articles enumerated in our letter of November 27, 1933, the following have been accepted:

Eli Lilly & Co.
- Ampoules Pentobarbital Sodium—Lilly 0.5 Gm. (7½ gr.)
- Ampoules Sodium Amytal 0.125 Gm. (1⅞ gr.) for Intramuscular Use (Lilly)
- Pulvules Sodium Amytal 1 Grain (Lilly)

National Drug Co.
- Antimeningococcic Serum, two 15 cc. double and ampoule vials packages
- Antimeningoccccic Serum, one 15 cc. cylinder package
- Antimeningococcic Serum, one 30 cc. double end vial package
- Diphtheria Toxoid, twenty 1 cc. vials package (ten immunization treatments)
- Rabies Vaccine-Human (Semple Method), four 2 cc. syringes and ten 2 cc. syringes packages
- Typhoid-Paratyphoid Combined Vaccine, 30 vial package (ten immunizations)
- Typhoid-Paratyphoid Combined Vaccine, 150 vial package (fifty immunizations)
- Typhoid Vaccine, 3 vial package (one immunization)

Schering Corporation
- Neo-Iopax
  - Ampoule Solution Neo-Iopax, 20 cc.

Sharp & Dohme, Inc.
- Antimeningococcic Serum, 30 cc. syringe package

Yours very truly,

PAUL NICHOLAS LEECH, *Secretary*,
Council on Pharmacy and Chemistry.

RECENT DEATHS

HUNT — LEMUEL JUDSON HUNT, M.D., a physician for many years in Roxbury, Massachusetts, died at the Massachusetts Memorial Hospitals, January 11, 1934.

He was born in Covington, Kentucky, February 26, 1847, and graduated from Pulte Medical College in 1873. He was a member of a Masonic Lodge, and the Pilgrim Fathers. He is survived by his widow, Mary J. (Loring) Hunt, and a son, William C. Hunt of Lynnfield.

CHUTE — ARTHUR LAMBERT CHUTE, M.D., of 350 Marlborough Street, died at his home on January 12 in his sixty-fifth year. He is survived by his widow, two sons, Dr. Richard Chute of Boston, Oliver Swift Chute of Whitinsville, and a daughter, Mrs. Samuel McMurtrie, Jr., of New York City.

HUBBARD — JOSHUA C. HUBBARD, M.D., died on January 9 at his home in Wayland, after a long illness. He was 64 years of age. Graduated from Harvard College in 1892 and from Harvard Medical School in 1896, Dr. Hubbard served for many years on the surgical staff of the Boston City Hospital. At the time of his death he was clinical professor of surgery, emeritus, of the Harvard Medical School.

SWAN — CHARLES LOUIS SWAN, M.D., of 30 Pearl Street, Stoughton, Massachusetts, died at his home December 31, 1933. He was actively engaged in the general practice of medicine up to the day of his death. He was born in Stoughton on December 17, 1867, the son of Dr. William Ellery Channing Swan and Estelle Parker Swan. He received his early education in the public schools but prepared for college at the Boston Latin School. He was graduated from Harvard College in 1891 and from Harvard Medical School in 1894. He was the third generation in his family to study medicine. After a year of postgraduate study abroad he became associated with his father in the general practice of medicine in Stoughton and the surrounding community.

He had various outside interests as is shown by the fact that he had been president of the Stoughton Gas & Electric Company before its merger with the Edison Company, and president of the Stearns Lumber Company of Bangor, Maine. He belonged to various clubs including the Harvard Club of Boston and New York, and was a member of the Masonic fraternity.

In 1896 he married Miss Josephine Cutler Stearns of Bangor, Maine, who survives him together with two sons, Dr. Channing S. Swan and Dr. Charles L. Swan, Jr.

JACKSON—DELBERT LINSCOTT JACKSON, M.D., 185 Buckminster Road, Brookline, with an office at 472 Commonwealth Avenue, died at his home January 1, 1934.

Dr. Jackson was born in Jefferson, Maine, November 22, 1881, the son of Mr. and Mrs. Manley A. Jackson. He graduated in medicine from the Medical School of Harvard University in 1908, and after an internship at the Boston City Hospital, served at the Boston Lying-In Hospital. He devoted himself to the practice of obstetrics.

He joined the Massachusetts Medical Society in 1911, and was a Fellow of the American Medical Association. He was a member of several clubs, fraternities, and medical societies.

He is survived by his widow Mrs. Florence Lyon (Fisher) Jackson.

TOLMAN—JULIA TOLMAN, M.D., a long-time physician of 695 Massachusetts Avenue, Arlington, Massachusetts, died at her home January 1, 1934, following a long illness. Dr. Tolman was born in Tewksbury, Massachusetts, April 24, 1853. She served as interne in the New England Hospital for Women and Children in Boston, and practiced in Arlington until within a few months of her death, and formerly was associated with the Symmes Hospital. She joined the Massachusetts Medical Society in 1886, and was a member of the Arlington Women's Club, and the 20th Century Club.

LUKER—JAMES C. LUKER, JR., M.D., of Hanover, Mass., died at the Cohasset Hospital on January 7, following an automobile collision. He was 32 years of age.

DARLING—EUGENE A. DARLING, M.D., of 33 Concord Avenue, Cambridge, died suddenly on January 9 at the age of 65. Dr. Darling, who was born in Troy, N. Y., was a graduate of Harvard College in 1890 and the Harvard Medical School in 1894. He was a Fellow of the American College of Surgeons. In 1892 he married Albenia Merrill of Cambridge. He is survived by his widow and four children.

MACDONALD—ALEXANDER A. MACDONALD, M.D., of Antigonish, Nova Scotia, died in that town on January 7. For nearly forty years he had been a practicing physician in Dorchester, returning to Nova Scotia about four months ago on account of ill health. He was born May 19, 1864, and received his early education in the Antigonish schools. He was graduated from St. Francis Xavier College in 1891 and completed his education at Georgetown University. He was unmarried.

NOTICES

THE MATAS AWARD

Invitations to attend the first presentation of the Matas Award in vascular surgery, created by the establishment of the Violet Hart Fund in the Tulane University, of Louisiana, have been issued. The presentation will be made by Dr. Mont R. Reid, of Cincinnati, Ohio, at Dixon Hall, Newcomb College Campus, at 8:30 P.M., on January 23, 1934.

THE AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

Examinations for Certificates

The American Board of Dermatology and Syphilology will hold written examinations for candidates for a certificate on April 30, 1934, in the following cities: New York City; St. Louis, Mo.; Boston, Mass.; Cleveland, Ohio; San Francisco, Calif.; Philadelphia, Pa.; Chicago, Ill.

If a sufficient number of applicants register for the examination from other districts, additional examinations will be held in other cities. This examination will be for applicants in both Group A and Group B.

The oral examination for both Group A and Group B will be held in Cleveland, Ohio, June 11 and 12, at the time of the American Medical Association meeting.

All applicants for a certificate who intend to take these examinations in either group must send their applications and other credentials to the office of the Secretary before March 14, 1934.

Application blanks and further information may be obtained from the Secretary, Dr. C. Guy Lane, 416 Marlboro Street, Boston, Mass.

RADIO HEALTH MESSAGES

January-February-March, 1934

Sponsorship: Public Education Committee of the Massachusetts Medical Society and Massachusetts Department of Public Health.

Courtesy WBZ. Fridays, 4:30 P.M.

Jan.
- 19 Hypertension
- 26 The Common Cold

Feb.
- 2 What A Parent Should Know About Measles
- 9 Milk
- 16 Stomach Trouble
- 23 Lumps in the Neck

March
- 2 Age and Cancer
- 9 Some Problems of Epilepsy
- 16 Fractures
- 23 How to Keep the Well Child Well
- 30 Résumé of the Year's Work

Health Question Box

Sponsored by Massachusetts Department of Public Health. Fridays 4:40 P.M.

Radio Health Forum

Queries from the public are answered under the sponsorship of the Department of Public Health.

Courtesy WEEI. Fridays, 5:00 P.M.

Questions on Health and Prevention of Disease may be sent to: Radio Health Forum, State Department of Public Health, State House, Boston.

Special

Beginning Friday, January 19, the State House Broadcasts will be discontinued and in their place will be substituted Ten Minute Health Reviews.

Sponsored by the Massachusetts Department of Public Health. Assisted by Miss Violette Babcock, Violinist, and Mr. G. Lambert Roscoe, Pianist and Organist.

Courtesy WEEI. Fridays, 1:15 P.M.

Glimpses into the History of Public Health in Massachusetts together with the Functions and Activities of the Massachusetts Department of Public Health, Blended with Classical Music.

After hearing this new program we would appreciate your comments.

REPORTS AND NOTICES OF MEETINGS

BOSTON ORTHOPEDIC CLUB

The December meeting of the Boston Orthopedic Club was held in the Boston Medical Library on Monday evening, December 11, 1933. The meeting was called to order by Dr. Arthur T. Legg, President of the Club, immediately following which the clinical program was begun.

Three papers were presented on the Intervertebral Disc, the first, "The Anatomy, Physiology, and Pathology of the Intervertebral Disc" by Dr. Robert Joplin, Orthopedic Resident Surgeon at the Children's Hospital. Dr. Joplin began by showing how the joints of the vertebral column differed from other joints of the body by not only acting as a means of motion, such as extension and flexion of the spine but also in taking up shocks upon the body and bearing the main weight of the body. Following this a discussion of the embryology of the intervertebral disc was taken up with the presentation of several slides from the Harvard embryo collection, the earliest of which was a slide from a human embryo six weeks of age. The speaker showed that the discs are made up of three portions, the annulus lamellosus, the peripheral portion of the disc; the nucleus pulposus, the main portion of the center of the disc; and the end plates, portions of the discs that come in contact with the central perforated plates of the vertebral bodies. Dr. Joplin stated that the discs were made up of a gelatinous material under a very

high pressure, since at autopsy when the thin capsule is cut the discs will extend out as though being pushed from behind. This fact was later shown to be of importance in rupture of the disc or prolapse of the disc, taken up further in the papers that followed. Next, two pathological conditions were considered, "High Discs and Low Discs," numerous slides being shown of the autopsy specimens and the x-ray films of cases in which the discs were much higher or lower than normal. Some discs were elevated so high and under such pressure, it seems, that they ruptured into the spongy portion of the adjacent vertebrae. Pathological conditions giving "high discs" are metastatic cancer, osteoporosis, and hunger pathology. This condition may appear at any age. As for the "low discs," the same group of pathological conditions may exist and Dr. Joplin further stated in relation to the "low discs" that this condition allowed the approximation of the bony surfaces which may result in "lipping" of the vertebrae or in bony fusion. Dr. Joplin concluded by stating that most of the work on the intervertebral disc from pathological and physiological standpoints had been done by Schmorl in Dresden, but that there is a great quantity of material at the Children's Hospital and the Massachusetts General Hospital from which the Boston group hopes to be able to put forward new facts concerning this subject.

The second paper was by Dr. Kenneth Coonse of the Boston City Hospital. Dr. Coonse discussed four cases which had come under his observation, in his practice. His first case was that of a man who entered complaining of pain in the lumbar portion of the spine, with radiation of the pain down the distribution of the sciatic nerves in the legs. He had previously had numerous operations for herniae. His last two had been under spinal anesthesia. Examination showed a very obese man with generalized tenderness over the lumbar spine and along both sides of the spinal column. Motions of the spine were within normal ranges and without very much pain. Finally an x-ray was taken which showed a bulging of the nuclei of numerous discs. With proper extension and braces the patient was subjectively relieved. His second case was that of a young laborer who suddenly had pain in the lower portion of his spine following the lifting of a very heavy weight. The patient was unable to stand up without marked pain and could not fully extend his back. There was localized spasm and pain over the lumbar spine. X-ray examination showed a rupture of an intervertebral disc into the body of one of the vertebrae. The speaker stated that it was impossible to state whether this rupture occurred as the result of the injury since he did not have x-rays before the injury.

His third case was of interest medico-legally. A workman fell and landed with great force on his outstretched legs. X-ray films confirmed the diagnosis of a compression fracture of one of the vertebrae. About six months later x-rays showed a rupture of one of the intervertebral discs. Whether the fracture or the rupture was the cause of his residual subjective pains, Dr. Coonse could not say.

The final paper was by Dr. Joseph Barr of the Massachusetts General Hospital who discussed the neurological aspects of rupture or prolapse of the intervertebral disc. Dr. Barr reviewed twenty cases from the records of the Massachusetts General Hospital, which had previously been diagnosed by operation or autopsy as chondroma of the canal, and found in going over the microscopic slides that these were not cases of actual chondromata, but presented the general appearance of the normal intervertebral discs, and that they were undoubtedly prolapsed portions or ruptured discs. Dr. Barr found that four of the cases were in the cervical region, four in the dorsal region, and twelve in the lumbosacral region. Symptoms in seven of the twelve cases in the lumbar region were stated to have resulted from trauma. Fifteen cases were in males, five in females. The clinical symptoms were shown to be due to pressure on the cord or the cauda equina, the main signs being pain (over the area of distribution of the nerves affected), and tingling sensations with numbness over the same parts. Later, atrophy set in and finally loss of motor power.

In the clinical investigation of the condition lumbar punctures were done, and in most of the cases the outstanding finding was an elevated total protein content of the spinal fluid. A combined cisternolumbar puncture sometimes showed partial block. Pathologically, seven of the pathological states have come from the annulus, four from the nucleus pulposus, and four were from both the portions of the discs.

Operation in these cases was followed, after removal of that portion of the disc that had prolapsed or ruptured and was pressing on the cord or the cauda equina, by relief in twelve instances, three showed no improvement, and three died as result of operation.

Following the presentation of these papers there was a general discussion. Dr. Mixter of the Massachusetts General Hospital, who had operated upon many of the cases, stated that it was a great surprise that the neurosurgeons had missed the proper diagnosis in this condition and called them chondromata for so long. From the practical standpoint he stated that most of the prolapses in the lumbar region were located in the lateral side of the canal. They appeared to be about pea-sized but upon cutting the capsule they became larger, and gave the appearance of being a fibrocartilaginous substance. He stated he had done several negative explorations in which the diagnosis of prolapsed discs had been made, and warned against doing this. Drs. Osgood, Wilson, Smith-Petersen, and Shortell added comments and constructive criticisms. Dr. Smith-Petersen stated that this was a new field and one that must be entered with great caution, inasmuch as, although Schmorl had found that 38 per cent of all his autopsies had shown the presence of abnormalities of the intervertebral disc, we had not yet

proved the condition to be one demanding exploratory laminectomy even though a pathological condition is suspected.

On the suggestion of Dr. Robert Osgood, a rising vote of thanks was given to each of the authors of these papers. The meeting then adjourned.

NEW ENGLAND HEART ASSOCIATION

The New England Heart Association held its third meeting of the year at the Boston City Hospital on the evening of December 12 at 8:30 P. M. Dr. Soma Weiss presided and opened the meeting with a presentation of pathological specimens recovered from several interesting cases.

The first case was that of a newborn baby that had slight cyanosis and a systolic murmur over the heart at birth. Thirty-six hours after birth the child was markedly cyanotic and died suddenly. At postmortem examination a rhabdomyoma was found which acted as a ball-valve at the mitral orifice.

The next case was that of a Negro janitor who had been treating for hypertension of 210-110, and who, during the previous year, had had three breaks in compensation. His heart weighed 1400 grams, the largest ever seen at the Boston City Hospital. Dr. Weiss emphasized that in this patient the hypertension was not so high as the hypertrophy might suggest, and that there appeared to be no relationship between the amount of hypertrophy and the height and duration of elevated blood pressure.

A third case showed a hypertrophy of the heart with an aneurysmal dilatation of the left descending branch of the coronary artery below which a thrombosis had occurred. The cardiac wall supplied by this artery was the seat of a mural thrombus which had given the patient no symptoms.

Dr. Weiss pointed out that in patients with a marked kyphosis of the thoracic spine, such as is frequently seen in tuberculosis of the vertebrae, the contents of the thoracic cage are distorted, leading to poor function of the organs. The heart from such a case showed marked hypertrophy of the right ventricle and an infantile lung.

The next case was that of a patient who was first seen in the out-patient department ten days before death, complaining of anginal pains with exertion. Four days before death he had symptoms suggesting a coronary attack. At postmortem a fairly well-organized hemopericardium was found and since the pathologist considered this to be older than four days, it is probable that the patient had sustained a small rupture of a coronary branch, which had healed only to be followed by a coronary occlusion.

Three cases of marked hypoplasia of the aorta were discussed. All had suffered from attacks of rheumatic fever and in none was the aortic hypoplasia diagnosed antemortem. Dr. Weiss feels that this condition is probably present from birth and predisposes to rheumatic infection. In considering the clinical symptoms in retrospect, he emphasized a small pulse, small blood vessels and fainting attacks as suggestive of this condition. All three of the cases suffered cardiac deaths due to rheumatic valvulitis.

Dr. James Faulkner next discussed certain experiments with dogs that were done to determine the effect of anaesthesia on the pulse and blood pressure relationship in acute hemorrhage. From these it was concluded: (1) When a dog is bled without anaesthesia, the pulse rate rises as the blood pressure falls, but with anaesthesia the pulse rate falls with the pressure after a brief preliminary rise. (2) With retransfusion of blood the pulse and blood pressure rise together. It is probable that the anaesthetic abolishes the sympathetic reflex which leads to an increased heart rate and allows the vagal action to predominate. The response to hemorrhage in an anaesthetized dog is similar to that seen in human beings who faint on a tilting table. The chart of a patient undergoing a long neurological operation was shown and corresponded exactly with results obtained in dogs under an anaesthetic.

Dr. David Davis considered "The Natural History of Rheumatic Heart Disease." From these studies of 113 cases who died as a result of rheumatic heart infection and in whom the onset of the first infection was fairly definite, it was concluded: (1) That if a person develops rheumatic heart disease after the age of 20 it is often the first infection, for five out of ten cases at necropsy examination showed only the signs of acute infection in the heart. (2) Of those cases who develop the disease before 11 or after 20, the former live longer in numbers of years after the initial infection. (3) One-third of the cases are dead in six months after the first decompensation and in one year one-half are dead. (4) From this study there are recognized four classes of decompensation, (a) acute decompensation with complete recovery, in which the prognosis is good; (b) a series of acute breaks in compensation in which the prognosis is bad; (c) decompensation of slow onset, in which recovery is fairly complete and the life expectancy is a few years; (d) failure is of gradual onset, recovery is fairly complete, but the patient survives the first break only a few months.

Dr. Eugene Ferris next presented the case history of a patient with Stokes-Adams' syndrome of neurogenic origin. A 64-year-old male entered the hospital because of attempted suicide with carbon monoxide gas. He had been having fainting attacks regularly with his meals. A diverticulum of the esophagus was discovered by x-ray and a balloon placed at the level of the diverticulum and when inflated produced typical fainting attacks with convulsions. The study of this reflex revealed the following: (1) Electrocardiographic tracings were typical of heart block attack when the balloon was inflated. At such times all of the ventricular beats recorded were ectopic in origin, and the block was therefore complete. (2) It was not connected with the carotid sinus mechanism. (3) Atropine in small doses, insufficient to slow the heart, blocked the reflex, although the blood pressure also dropped upon inflation of the balloon. These results suggest that atropine may have an effect other than on the mo-

tor endings in the heart and also that the fainting was due to a mechanism quite separate from the drop in blood pressure. (4) Adrenaline and ephedrine abolished the reflex and although the electrocardiogram showed ectopic beats, they were fairly close to normal in their spacing. (5) Barium chloride, 30 mg. b.i.d. had no effect when taken for two weeks. (6) Because of the close association of the cerebral circulation to that of the face, and because this patient showed blanching of the face when in a typical attack, it was suggested that the fainting is due to constriction of the cerebral vessels.

Dr. Richard Capps demonstrated two cases of carotid sinus reflex. The first was that of a 42-year-old male who entered the hospital with a complaint of attacks of dizziness and fainting with convulsive movements. Pressure on the left carotid sinus produced a slight fall in pulse rate and blood pressure, and pressure on the right a slightly greater fall, with fainting and convulsions. The patient was demonstrated in a typical attack when pressure was produced over the right carotid sinus.

The second case was interesting in that pressure over the right sinus produced a fall in systolic pressure from 115 to 85 mm. of mercury, but no fainting, while pressure on the left gave fainting but no drop in pressure, showing that the fainting mechanism is more complex than a simple drop in blood pressure. In conclusion the speaker stated that they are coming to regard this condition as an abnormality of the vegetative nervous system.

Dr. Timothy Leary was the final speaker. He discussed "Arteriosclerosis of the Coronary Arteries." The speaker showed some excellent slides of diseased coronary arteries from human beings, and from rabbits that had been fed on high cholesterol diets. In the human being the following types of coronary sclerosis are found: (1) That occurring in relatively young persons in whom there are relatively few or no symptoms, but who die suddenly from coronary occlusion. In them there is marked fibrosis of the coronary walls formed in response to subepithelial inflammation with fibrin deposits about cholesterin crystals. (2) The form which is seen in people over 47 years of age and characterized by lipoid cells which break down and lead to fibrosis as well as the so-called atheromatous abscesses. Several slides were shown demonstrating the rupture of these abscesses into the lumen of the coronary artery.

In rabbits fed on a high cholesterol diet the changes in the coronary vessels are practically identical with those seen in the human being. Dr. Leary believes that in human beings there is variability in the capacity to handle cholesterol, and that if the tolerance is low, arteriosclerosis results. The localization of this process in the coronary arteries is dependent upon some peculiar predisposition. We have an analogy here in the diabetics who have been shown to develop arteriosclerosis much more readily when placed on a high fat diet.

In rabbits with normal thyroid glands potassium iodide will prevent the formation of fat cells in the subendothelial tissue of the coronary vessels and the resultant fibrotic processes. Alcohol so far has had no effect in preventing the development of coronary sclerosis.

ESSEX NORTH DISTRICT MEDICAL SOCIETY

The Ninety-Third Semi-Annual Meeting of the Essex North District Medical Society was held on January 3, 1934, at the Elks' Club Rathskeller in Haverhill, with 53 present at dinner, about a dozen more Fellows arriving later.

On motion of Dr. Burnham, duly seconded, it was voted that each member contribute fifty cents toward the dinner and the society pay the balance.

At 1:30 the business meeting opened with the meeting called to order by the President, Dr. Coffin. The minutes of the previous meeting were read and approved. Dr. Durant read memorials on Dr. I. J. Clarke, deceased. Dr. Still read memorials on Dr. H. Murray Crittenden, deceased. Dr. Bagnall reported on recent activities of the Public Relations Committee of the parent society. It was moved by Dr. Burnham, seconded and so voted, that the A. M. A. auto emblem be adopted by the society as official in order to facilitate traffic and parking advantages needed by the doctor.

There was an active discussion about rates under the Federal Welfare Plan and also about the proposed exclusion of the family physician in Civil Works injuries. Dr. Burnham reported that the latest information indicated that the family physician was to be the one authorized to furnish medical care under Civil Works except where a Federal Hospital was available. Dr. Horne moved to indorse and support action already taken and to be taken by the Public Relations Committee of the Massachusetts Medical Society. The motion was seconded and unanimously adopted.

Owing to the illness of Hon. Richard K. Conant, Commissioner of Public Welfare for the Commonwealth of Massachusetts, Dr. Leader of that department presented some facts and opinions relating to Bulletin 7 as it concerns the doctor in general practice, city physicians and departments of public welfare. Dr. Leader said that his department was now waiting a report from the Massachusetts Medical Society regarding fee schedule for federal welfare cases. He said that there was as yet no money available or machinery to pay, as Massachusetts has used some of these funds for reduction of taxation and they may have to be returned by the municipalities involved. After the fee policies and machinery have been decided upon by the Massachusetts Medical Society, it is anticipated that they will be approved by the Federal Welfare Administrator and after other important details are arranged a new plan will commence operation. Dr. Leader said Bulletin 6 and Bulletin 3 needed to be read in connection with Bulletin 7. Under provisions of Bulletin 3 this relief is to be extended

to all needy who do not earn sufficient income to take care of medical expenses. These cases are not confined to those under public welfare so long as they satisfy the local Board of Public Welfare that they have not sufficient funds to meet the expenses of illness. Bills should be submitted within ten days from the first of the month following completion of treatment and moneys will be paid from the Federal funds direct. He discussed relationship of city physicians to this scheme calling attention to the fact that the Town of Adams had discontinued the city physician, providing for care by the family physicians at the following rates: office $1; house $2 to $2.50; tonsillectomy $15; confinement $25; major operation $50; with anesthesia added. He indicated the probable need of a committee in each political subdivision to take care of any abuses that might arise. He expressed it as his opinion that there should not be any undue rush about the submission of plans by the medical society because the arrangement was probably here to stay. He indicated that owing to lack of organization of the dental society (only 50 per cent of the Massachusetts dentists are members of the state society) they were at a disadvantage because the Bulletin states that the plan shall be drawn and adopted by organized medicine. The dentists under this plan so far could provide only emergency treatments such as extractions. There was active discussion by Drs. Whitney, O'Reilly, Barclay, Benson, Popoff, Durant and Perkins.

The President announced that a fee committee had been appointed at the request of the President of the Massachusetts Medical Society which included Drs. Durant, Hurd and Barr. Dr. Durant reported progress, submitting the rate of $1 to $1.25 in the office; $2 in the home; $4 at night; obstetrical, prenatal and postnatal $25, average. This was discussed by Drs. Perkins, Sweetsir, Burgiel, Benson, Horne, and Armitage. Dr. Burnham then moved that the President appoint a committee including the President and Secretary, Drs. Durant, Hurd and Barr and one from each otherwise unrepresented town or city in the district to work with the Public Relations Committee of the Essex North District Society on fees and policies for submission to the President and Council of the State Society at the February meeting. This motion was seconded by Dr. Hubbell and unanimously adopted, after discussion by Drs. Armitage, Connor, Baketel and Sweetsir. An amendment proposed by Dr. Popoff providing that each city and town choose its own representative failed of adoption.

Dr. Joseph O'Reilly, of Lawrence, portrayed the hardships of the ward physicians in Lawrence. Each ward physician has two wards, the two which he supervises comprise forty-three thousand people and yield an average of $6.54 a week to the physician. Twenty-four-hour duty and a lack of proper consideration by the Welfare Officer make the position very unremunerative. He cited an increase in applications, each application being good for thirty days, from 312 in 1929 to 985 in 1933, with a reduction of 15 per cent in the pay provided for all the work. The first two months of 1933 averaged a gross yield of between five and ten cents per call.

Dr. Bartley, a Lawrence school physician, reported a salary of $600 less 15 per cent, visits to the school with clinic between 11 and 12, twice a week. Twenty thousand school children are taken care of by six physicians. He cited instances where the heads of the family earn $90 a week and are getting free vaccination, immunization and tonsillectomy.

Dr. Radcliffe, one of the two city physicians of Haverhill, receiving $900 a year, reported that the first three months yielded him a gross average of 14½ cents a call and he found that he had an expense of 22 cents per patient for medicine alone. During the year he had had 5600 patients with an average of two office and one house call each. The city now allows ten dollars in addition for each home confinement to lessen the number of hospital confinements. The year averaged 15-9/10 cents per patient visited.

Dr. Sweetsir, of Merrimac, stressed the fact that the physician is the only man discounting his bills, the grocer and coal man, for the most part getting regular rates. He reported that the Town of Merrimac had a $48 tax rate last year and $20 of that $48 was covered by welfare costs. Twenty-two hundred dollars was paid to the two physicians in the town for welfare work and they are working under 25 per cent discounts arrangement temporarily.

Dr. Blais, of Amesbury, city physician, receives a salary of $700 averaging a little better than 25 cents per call. He reported a very interesting and effective method which has eliminated 90 per cent of the night calls. The patient understands that the cost of medicine will be deducted and a penalty of one day's labor in the street department, if the night call is not of an emergency nature. He recommended the abolition of the town physician.

Dr. Stockwell, city physician of Newburyport, reported that about 28 per cent were receiving welfare aid on the first of December, 1933. Of this 28 10 per cent are looked out for by the city physician, about 3 per cent by the soldiers' relief physician; the rest are provided care by general practitioners without remuneration. The gross receipts per call of the city physician average thirty-four cents.

FAULKNER HOSPITAL CLINICAL MEETINGS

The usual monthly meeting was held at the Faulkner Hospital on Thursday afternoon, January 4, at 5:00 P. M. Despite the unfavorable weather conditions the meeting was unusually well attended. Two cases which had come to autopsy during the month were discussed.

One case had died of miliary tuberculosis following an illness in bed of only three weeks. The illness started four months before with pain in the back which turned out to be due to tuberculosis of the dorsal vertebra with a cold abscess. Despite

this condition there was no tenderness over the spine on percussion in this area, nor did the patient have any difficulty in sitting up in bed. The distribution of the miliary tubercles in the lungs was another point of interest, because the upper lobes of both lungs were quite free of the tubercles on gross inspection while both lower lobes were well studded. Although on gross inspection the other organs of the body apparently did not have any tubercles in them; upon microscopic examination minute tubercles were scattered throughout all the organs. The exact portal of entry of the tubercle bacilli into the blood stream was not discovered but it is presumed that it was associated with the lesion in the spine.

The second case was one of sepsis extending from a small furuncle on the nose into the cavernous sinus and producing in addition a basilar meningitis. The special point of interest was the fact that, although there was some exophthalmos of the eye on the side of the cavernous sinus thrombosis, the nerve had on that side appeared normal. This case emphasized the importance of infections in the soft tissue around the upper lip and nose.

Dr. W. Richard Ohler then gave a very interesting talk on the question of hypothyroidism, especially in those cases in which the usual symptoms of myxedema are not present. He cited several interesting cases with symptoms of fatigue, nervous irritability, menstrual disorders and other vague symptoms in which there was distinct improvement upon the administration of thyroid extract. He called attention to the fact that probably some diagnostic aid could be obtained by the examination of the cholesterol in the blood in suspected cases of thyroid deficiency. Usually as the metabolic rate drops in cases of thyroid insufficiency the cholesterol in the blood increases. Therefore, if the cholesterol in the blood is not increased in a case with a lowered basal metabolism, one should be suspicious that the low metabolic rate may not be due to thyroid insufficiency. He also cited some very striking cases in which there had been a low metabolic rate and symptoms in which the administration of thyroid was of no benefit but in which improvement in symptoms occurred and the basal metabolic rate returned to normal after the removal of foci of infection or the reorganization of the patient's habits of life. In other words, other factors than a thyroid deficiency may cause a low metabolic rate and this rate may return to normal by the elimination of these factors without the administration of thyroid.

The next monthly meeting will be held on Thursday afternoon, February 1, 1934. In addition to the usual pathological conference on the cases which come to autopsy during the month Dr. James R. Torbert will give a short talk on "The Treatment of Obstetrical Hemorrhage." All members of the profession are invited to attend.

MASSACHUSETTS CENTRAL HEALTH COUNCIL

Annual Meeting

The Annual Meeting of the Massachusetts Central Health Council will be held at the Whittier Street Health Unit on Thursday, January 25, at 4:00 o'clock in the afternoon. "Mouth Health and Its Significance in the Health Picture" will be the theme of the meeting.

Dr. LeRoy M. S. Miner, Dean of Harvard Dental School, Dr. Henry D. Chadwick, State Commissioner of Public Health, Dr. E. Melville Quinby, President, Massachusetts Dental Hygiene Council; Dr. Warren R. Sisson, Chairman, New England Division, American Association of Pediatrics, and Dr. Frank A. Delabarre, Lecturer at Harvard Dental School, will be the speakers.

The Central Health Council is a federation of Official and Voluntary Health Organizations in the Commonwealth. Professor Curtis M. Hilliard, Head of the Department of Biology and Public Health of Simmons College, will preside.

Physicians, nurses, social workers and others interested in public health are invited to the meeting. There will be no tickets of admission.

Dr. Charles F. Wilinsky, Deputy Commissioner of Public Health and Director of the Division of Child Hygiene of the Boston Health Department, will welcome the Council and its friends to the new Health Unit.

NEW ENGLAND HEART ASSOCIATION

The fourth meeting of the New England Heart Association will be held in the Auditorium of the Beth Israel Hospital, Monday, January 29, at 8:15 P.M.

All members of the New England Heart Association and interested physicians are invited to attend.

Paul W. Emerson, M.D., *Secretary.*

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held in the Peter Bent Brigham Hospital Amphitheatre (Van Dyke Street entrance), Tuesday evening, January 30, at 8:15 o'clock.

Program

Presentation of Cases.

"The Advantages to the Harvard School of Public Health of a Distinguished Ancestry." By Reginald Fitz, M.D.

"The Beginnings of Microscopy at Harvard:—The Hollis Gift of a Microscope (1732): Observations by Edward Bromfield Toward 1746." By Frederic T. Lewis, M.D.

John Homans, M.D., *Secretary.*

SOCIETY MEETINGS, CONGRESSES AND CONFERENCES

January 18—Boston City Hospital, Staff Clinical Meeting, 8:15 P.M. in the Thorndike Amphitheatre.

January 18—New England Hospital for Women and Children at 8 P.M.

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January 19—Sources of Information. James F. Ballard.

January 23—Sources of Information. James F. Ballard.

January 30—How to Go about the Investigation of a Medical Subject. Dr. W. C. Quinby.

February 6—The Making of Medical Books. Dr. Henry Viets.

February 13—Incunabula. James F. Ballard.

Tuesdays at 8 P.M. except for the second meeting, which will be on Friday, January 19.
Boston Medical Library, 8 The Fenway.

January 25—Massachusetts Central Health Council. See page 173.

January 29—New England Heart Association. See page 173.

January 30—Harvard Medical Society. See page 173.

February 1—Faulkner Hospital Clinical Meeting. See page 172.

February 7—Annual dinner of the Tufts College Medical School Alumni Association at the Boston City Club, 6:30 P.M.

February 12—House Officers' Association of the Boston City Hospital. Subject: "Forensic Psychiatry". Speakers: Dr. A. Warren Stearns and Dr. Abraham Myerson.

February 16 and 17—The New England Hospital Association is holding its Twelfth Annual Meeting at the University Club, Boston. For details write Dr. A. G. Engelbach, Massachusetts General Hospital, Boston.

April 16-20—The American College of Physicians will hold its Eighteenth Annual Clinical Session in Chicago at the Palmer House. For information write Mr. E. R. Loveland, Executive Secretary, 133-135 South 36th Street, Philadelphia, Pa.

April 30—The American Board of Dermatology and Syphilology. Examinations for Certificates. See page 168.

July 24-31—The IVth International Congress of Radiology will be held in Zurich under the presidency of Professor H. R. Schniz. General Secretary Dr. H. E. Walther, Gloriastrasse 14, Zurich.

September 3-6—American Public Health Association, at Pasadena, California. Dr. J. D. Dunshee, Chairman, Local Committee on Arrangements.

September 4, 5, 6—International Union Against Tuberculosis will be held in Warsaw. For particulars address The National Tuberculosis Association, 450 Seventh Avenue, New York, N. Y.

DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH DISTRICT MEDICAL SOCIETY

February 7—Council Meeting, Boston.

Wednesday, March 7—Lynn Hospital. Clinic 5 P.M. Dinner 7 P.M. Speaker Dr. Frank H. Lahey, Boston. Subject to be announced. Film Electrocardiogram.

Wednesday, April 4—Essex Sanatorium, Middleton. Clinic 5 P.M. Dinner 7 P.M. Speakers: Dr. Elliott P. Joslin and Dr. Howard F. Root, Boston. Subject: "Tuberculosis Complicating Diabetes."

Thursday, May 3—Censors' Meeting, at Salem Hospital, 3:30 P.M.

Tuesday, May 8—Annual Meeting. Salem Country Club, Forrest Street, Peabody. Dinner at 7. Speaker to be announced. Subject to be announced.

RALPH E. STONE, M.D., Secretary.
221 Cabot Street, Beverly, Mass.

FRANKLIN DISTRICT MEDICAL SOCIETY

Meetings will be held on the second Tuesday of March and May at the Weldon Hotel, Greenfield, at 11 A.M.

CHARLES MOLINE, M.D., Secretary.
Sunderland, Mass.

MIDDLESEX EAST DISTRICT MEDICAL SOCIETY

Meetings will take place in March (2nd Wednesday) at Wakefield, and May (2nd Wednesday) at Winchester.

ALLAN R. CUNNINGHAM, M.D., Secretary.
76 Church Street, Winchester, Mass.

MIDDLESEX NORTH DISTRICT MEDICAL SOCIETY

Meetings will be held on January 31, and April 25

T. A. STAMAS, M.D., Secretary.
226 Central Street, Lowell, Mass.

MIDDLESEX SOUTH DISTRICT MEDICAL SOCIETY

February 20—Meeting at the Metropolitan State Hospital, Waltham, 5 P.M.

NORFOLK DISTRICT MEDICAL SOCIETY

January 28—Tentatively Roxbury Masonic Temple, 8 P.M. Continuance of Symposium on Diseases of the Blood. Dr. Dameshek and Dr. Straus.

February 27—Place, time, subject, and speaker to be announced.

March 27—Place and time to be announced. Dr. Edward A. Edwards and Dr. Henry H. Faxon. Symposium on the Treatment of Varicose Veins.

May—Annual Meeting. Place, time and program to be announced.

FRANK S. CRUICKSHANK, M.D., Secretary.
1695 Beacon Street, Brookline, Mass.

NORFOLK SOUTH DISTRICT MEDICAL SOCIETY

February 1—12 noon at Norfolk County Hospital. Stated Meeting. Speaker: Dr. Sara Jordan. Subject: Stomach Ulcers.

March 1—12 noon at Quincy City Hospital. Program by the hospital staff.

April 5—12 noon at Norfolk County Hospital. Speaker: Dr. Elliott P. Joslin. Subject: Diabetes.

May 3—12 noon at Norfolk County Hospital. Annual Meeting. Election of Officers.

N. R. PILLSBURY, M.D., Secretary.
Norfolk County Hospital, South Braintree, Mass.

SUFFOLK DISTRICT MEDICAL SOCIETY

January 31—General Meeting in association with the Boston Medical Library and the Trudeau Society. Speaker: Dr. Lawrason Brown of Saranac Lake.

March 28—Clinical Meeting at the Massachusetts Memorial Hospitals.

April 25—Annual Meeting at the Boston Medical Library. Election of Officers. Scientific Program, titles and speakers to be announced.

The Medical Profession is cordially invited to attend all of these meetings.

JAMES H. MEANS, M.D., Vice-President.
GEORGE P. REYNOLDS, M.D., Secretary,
311 Beacon Street, Boston, Mass.
ALEXANDER S. BEGG, M.D.,
Boston Medical Library.

WORCESTER DISTRICT MEDICAL SOCIETY

All meetings to be held on Wednesdays as follows:

February 14—Dinner and scientific program at the Worcester State Hospital, Worcester, Mass.

March 14—Dinner and scientific program at the Memorial Hospital, Worcester, Mass.

April 11—Open date.

May 9—Annual Meeting. Time and place to be announced later.

ERWIN C. MILLER, M.D., Secretary.
27 Elm Street, Worcester, Mass.

BOOK REVIEW

Essentials of Prescription Writing. By CARY EGGLESTON, M.D., Assistant Professor of Clinical Medicine, Cornell University Medical College, New York City. Fifth Edition, Revised. Philadelphia and London: W. B. Saunders Company, 1933. 155 Pages. Price $1.50.

The appearance of this new edition, amplified but not materially changed, requires little comment except to say that it deserves continued popularity. It is an admirably complete yet concise presentation of a subject in which many students and also many physicians are deficient.